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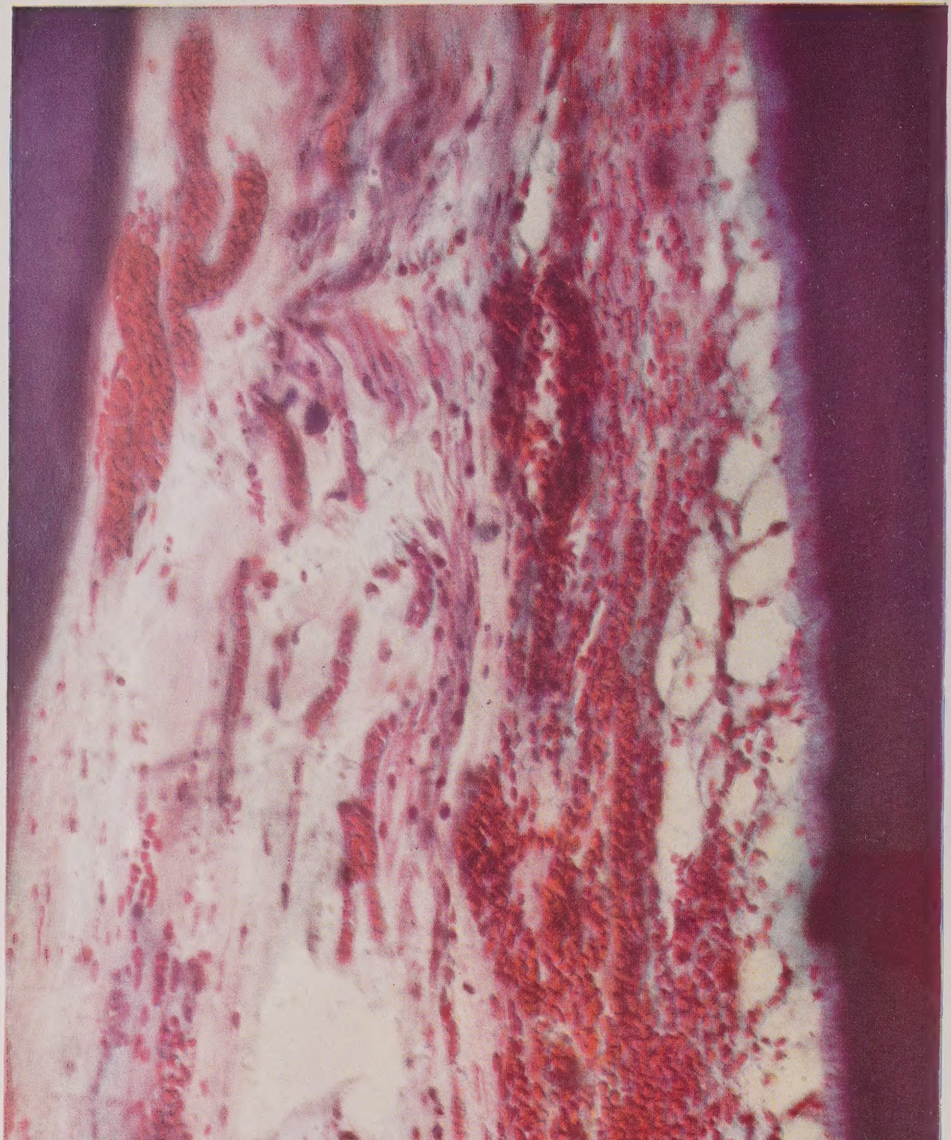
VOLUME I

RESEARCHES ON ORAL AND SYSTEMIC EXPRESSIONS OF DENTAL INFECTIONS



ACUTE PULPITIS.

Symptoms—Hypersensitiveness to thermal change. Histopathology—Interstitial hemorrhage into dental pulp from infected caries.

Frontispiece Vol. I.

DENTAL INFECTIONS
ORAL AND SYSTEMIC

(VOLUME I)

BEING A CONTRIBUTION TO THE PATHOLOGY OF DENTAL INFECTIONS
FOCAL INFECTIONS, AND THE DEGENERATIVE DISEASES

By

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The American Dental Association
(Discontinued)

THIS IS THE EXPERIMENTAL BASIS FOR VOLUME II
"DENTAL INFECTIONS AND THE DEGENERATIVE DISEASES"

VOLUME I PRESENTS

RESEARCHES ON FUNDAMENTALS OF ORAL AND SYSTEMIC
EXPRESSIONS OF DENTAL INFECTIONS

VOLUME II PRESENTS

RESEARCHES ON CLINICAL EXPRESSIONS
OF DENTAL INFECTIONS

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To

MR. AND MRS. FRANCIS E. DRURY
MY ESTEEMED FRIENDS

IN APPRECIATION OF
THEIR KINDLY ENCOURAGEMENT AND HELPFUL INTEREST
THIS VOLUME IS AFFECTIONATELY DEDICATED

A New Truth a New Sense

"THE acquisition of a new truth is like the acquisition of a new sense, which renders a man capable of perceiving and recognizing a large number of phenomena that are invisible and hidden from another, as they were from him originally." LIEBIG. *Chemische Briefe*

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PREFACE

THE PURPOSE of these two volumes is to present new data and important new interpretations suggested by them. I wish to assure the readers of these volumes that I am not unmindful of the tremendous responsibility that is involved in my presuming to furnish to the medical and dental professions a new interpretation of the pathology of oral and systemic expressions of dental infections and of their role in the production of the degenerative diseases. Notwithstanding this great responsibility, however, I have a sense of deep confidence that the new interpretations, I am herewith presenting, more adequately harmonize the available evidence and clinical findings than do any that we have had heretofore.

This title presumes that dental infections have been demonstrated to be an important contributing factor in the production of the degenerative diseases. I have no hesitancy in leaving to the evidence herewith submitted, whether I am justified in using this title; and now that we see it in the new light, we understand with a kindly sympathy the misapprehensions and the causes for the confusions of the past. It is probable that there seldom has been and seldom will be in the history of humanity, so universal a misapprehension based upon misconceptions, if we may judge importance on the merit of factors involved. Briefly stated, this misapprehension has been this. We have mistaken effect for cause. Since everything is relative, infection has had to have a quantity factor, and that quantity factor has had to be measured. The measure has been the structural change at the point of the focus. This has presupposed that quantity and virulence of organism, on the one hand, determined in large part the danger to the host. With this as the fundamental, it has been practically universally conceded that comfort and serviceability were dependable symptoms of safety and efficiency. But this being the fundamental conception, it has been most natural that exceptions to this rule would challenge the presumption that a large enough quantity of dental infections would do harm, whereas a small quantity would not. There has, accordingly, been a paradox that heretofore has been unanswered, and which probably has been the basis for nearly all of the opposition to the proposition that dental *infections could do systemic harm. Such a one has been the following:*

In the various out-clinics of hospitals and in such groups where large numbers of individuals could be observed, it has been continually noted that those individuals with apparently the largest quantity of pus exuding from infected roots, and particularly from apical fistulæ, had no rheumatism, heart, or kidney involvement; and in those cases where these lesions did exist, there was no such evidence of discharge. If, then, these individuals with so much infection were not involved, why strain the point so far as to assume that less infection was the cause in these other individuals? The fundamental conception has been wrong, for the individual with the large quantity of pus, as evidenced by the flowing fistulæ, did not necessarily have more infection that those of the other group who, with similar conditions, had no such physical expressions. The difference is in the individuals of the two groups, and this is one of the important new truths that these volumes will bring, and is a difference in the capacity for reaction. The teachings of the past have assumed that there was a distinct difference in the attacking power and virulence as well as the quantity factor involved in different dental infections. These reports will show that our problem is not one, primarily, of the morphology and biological characteristics of the strain involved, but, on the contrary, any strain of the streptococcus group, which may chance to get into that environment, will tend to produce the same unit characteristics, and that these characteristics will, because of the very great adaptability of these organisms, be the resultant of the pabulum furnished by the host as the culture medium for the strains involved.

Further, I have shown that an individual's defense for the streptococcal group of infections is primarily a matter of a special defensive factor or mechanism for the streptococcus group, which factor he inherits from his ancestry just as he inherits all his other unit characters, that this quality has a unit basis in relation to individual organs quite independent of the entire body. This normal defensive factor is a relative one and is subject to modification through a wide range as a result of overloads. The individual, therefore, with a high defense, expresses that defensive capacity immediately about the tooth, for he efficiently resists the invader immediately about the point of entrance. This warfare will be shown to be a matter of the establishment and maintenance of a local and systemic quarantine, the mechanisms for the development and maintenance of which are brought out in succeeding chapters. I have shown that these very defensive factors are all measurable and can be expressed *quantitatively by chemical analyses of various factors of the blood and by determining the bactericidal properties of the blood. It is a most significant and lamentable fact, that there has been practically no important progress in our understanding of the etiology of periodontoclasia, or pyorrhea alveolaris, of the etiology of dental caries, or of the true relation of dental infections to systemic disease except in the most general terms, in a whole century, and this, fundamentally, because the accepted doctrines had no basis in experimental pathology, but were a matter of inheritance from preceding generations and were the logical assumptions. These new interpretations, which I furnish herewith, as well as the data from which I have drawn them, adequately explain the dental paradoxes as being precisely what we should have expected, and as being in complete harmony with this newer view.*

This work must stand or fall absolutely on its merits in this regard, and I have no hesitancy in sending this bark out into the storm which I know must follow, and I have no desire that it shall weather the storm if its cargo is not entirely that of truth. The very large scope of the presentation precludes the possibility of the detailed argument and presentation of data that will be desirable simply in a critical review. I have, accordingly, undertaken to make this serve the double purpose of being directly applicable to clinical practice (for it has grown out of the most exacting and intimate study of clinical relations) and to furnish an adequate amount of experimental data to establish and justify the new interpretations. The data, that I am furnishing, are only a small fraction of what I have available.

With regard to the timeliness of such a message, there is no question or doubt.

This can perhaps best be summarized by suggesting the present stage of advancement of general medical and dental knowledge. This was splendidly done at the recent meeting of the American Association for the Advancement of Science (Boston, December 26-30, 1922) when a general session was addressed by Dr. Livingston Farrand, president of Cornell University, on the subject, "The nation and its health." Science, in abstracting his address, stated:

"Dr. Farrand reviewed the progress of public health work in this country and pointed out that since 1870 the average length of life has been increased by fifteen years, that marked reduction has occurred during this period in infant mortality and in mortality due to tuberculosis, typhoid, smallpox and many other diseases. The efforts of health workers and organizations have, however, been unable thus far

to prevent increases in certain unconquered diseases, such as cancer and diseases of the heart and kidneys. The most outstanding problem at present concerns the control of the degenerative diseases of later life, an increase in mortality from these being an inevitable consequence of improvements in the control of diseases of infancy and youth."

If, as I interpret these researches to demonstrate, the degenerative diseases to which he refers, particularly of the heart and kidneys, are very markedly increased in their severity and in many instances actually caused by dental focal infections, there probably is no more important problem for our modernly civilized communities than the study of means for the prevention, in every way possible, of these degenerative processes.

Few, if any, of the contributors to medical science have shown a greater appreciation of this need and deserve greater credit for the danger signals given to the profession and humanity, than Sir William Hunter. In a recent discussion by him before the Medical Society of London (December 11, 1922) he called attention to the fact that the present discussion in which he was taking part was the first which had taken place on oral sepsis before that society since the subject originated in its newer phase in the paper presented by him before that society twenty years ago. In the paper which he was discussing Sir William Willcox had given a general resumé of the literature without new experimental data and had stated that he agreed with Dr. Beddard who had expressed the opinion that 90 per cent of the non-specific infective arthritis cases were due to infection arising from the teeth. Lord Dawson in closing the discussion stated that the subject afforded a very good example of a necessity for teamwork, that what was wanted was some really connected work upon the subject to which dentists, radiographers, and bacteriologists would all contribute.

In conducting the researches herewith reported, I have undertaken to secure the closest coöperation possible by engaging men for my staff, whose exclusive attention has thereby been concentrated on the particular phase for which they were engaged. There has, therefore, been the closest possible coöperation without the possibility of distraction or conflicting purpose; and I am profoundly indebted to these collaborators, who have been many, during these two and one-half decades, in working on these problems.

No work on this subject can be presented at this time, if at any time in the future, without recognizing in a very important way the *exceptional pioneer work that has been done by Dr. E. C. Rosenow, first while working in Chicago at the Presbyterian Hospital in association with Dr. Frank Billings, and latterly in the Mayo Institute at Rochester, Minnesota. Probably to Dr. Billings more than to any other American internist is due the credit for the early recognition of the importance of streptococcal focal infections in systemic involvements, for his work practically paralleled that of Sir William Hunter in England.*

I wish to express my deep indebtedness to all these pioneers in this field; and if my work shall have removed some of the confusions which have been largely responsible for the lack of appreciation of, and opposition to, the efforts of these great pioneers, I should be doubly glad because of my esteem for their courage in the midst of the bitterest of opposition, and also for the larger helpfulness that may come to humanity by a more universal medical and dental appreciation of this need. There could not possibly be a stronger tribute to the sincerity of these men than that they should so persistently follow the line of their conviction in the midst of the unprecedented antagonism, for theirs was the vision of a great new truth.

It is my judgment that the most important phase of this contribution will not be simply the correcting of a misconception of fundamental dental pathology, but the making of an important new contribution to the pathology of focal infections and the dengerative diseases. In the light of the succeeding chapters there is strong evidence that the degenerative processes which we have thought of as various diseases, such as Bright's disease, heart disease, nervous system involvement, digestive tract disfunction, etc., etc., are primarily the end products of disturbed processes of metabolism and catabolism, and that an important contributing factor to these disfunctions will be found to be focal infection, whether of dental or other origin. Since, however, they develop most largely in adult life, more than 95 per cent of the members of the human race will be found to have a source in the form of an infected non-vital tooth for the disturbers of the hormones which control organ and tissue functions. The evidence in these chapters will take the form of the measurement of these factors, the reproduction of the various cycles of animal experimentation, and numerous evidences of the elimination or betterment of the human physical disfunction and organ degeneration following the removal of the dental infection.

While the preparation of this text has involved a series of researches extending over more than twenty-five years, it has not seemed to me *wise to publish a less complete statement for the following reasons:*

The earlier researches involved seemed to establish that the current fundamentals, as universally accepted, were not based on truth; and I soon learned from the presentation of papers and illustrated lectures that the bringing to the profession of a negative statement, simply challenging the old fundamentals without putting something in their place, was a very unwelcome message. The role of an iconoclast is seldom, if ever, a happy one.

Second, while it was a relatively simple matter to demonstrate that the accepted fundamentals were in error, it has been a tremendously difficult matter to develop new working hypotheses that would stand the most critical test that I have been able to put to them.

Third, a new interpretation must, by the very nature of things, and it is well that it is so, run a gauntlet of intensive criticism, which not only is right, but becomes a purifying fire; for only by the most exacting tests should new truths presume to supplant old ones.

It is a matter of deep regret to me that so much of my energy has had to be expended in the business side of dentistry in order that the means might be available for conducting these investigations, which has not left an adequate amount of time and strength to perfect these volumes to a greater degree.

It has been impossible because of the voluminous presentation, for me to include an historical review and bibliography for each chapter, which, in themselves, would add many hundred pages.

These researches have required the use of approximately five hundred rabbits a year, for several years; and, for those who would criticize their use, I wish to state that many of these rabbits have in my judgment made a far greater individual contribution and service to the welfare of humanity than hosts of human beings. Rabbits that run wild and are chased by their enemies have not been as well fed and as happily housed, or been privileged to die under chloroform. I have had many patients express their gratitude and confidence by offering themselves for any experiments that I would care to try upon them, if, by so doing, they too could help humanity. The greatest tragedy that I see in the whole development of this subject in the past, has been that humans alone have been used as the experimental material and the experiments have not been properly checked; for it has been considered that comfort and serviceability were a sure proof of the success of the experiment, entirely misapprehending that a lack of reaction about the tooth, and the consequent comfort, only meant that the quarantine was not in operation and the toxin and bacterial invasion *were passing to other parts of the body, there to break down tissue and shorten life.*

I am deeply indebted to many persons for assistance in the development of this work. First of all, I want to pay the highest tribute possible to the patients who have given me every possible coöperation. While I have no doubt they felt a gratification for relief given them from distressing symptoms, and distinct improvement in health and comfort of living, the spirit in which they have coöperated not only by paying liberally for the services as they were charged to them, but by material contributions made in many instances to the work, without which it could not have been so efficiently conducted. For those who are unfamiliar with the unusual expense of this type of work, it will be of interest to note that the research work involved in these two volumes has cost in excess of $250,000, which has been provided almost entirely by the fees from the patients.

I wish especially to thank all the members of my staff averaging sixteen in the last three years, and seldom less than five during the preceding twenty-five years in which I have been doing this work. It is true that we have had a common joy in this service to humanity, but I cannot pay too high a tribute to the earnestness and completeness with which they have joined in the search for these new truths. I cannot imagine a greater joy in any enterprise than that which they have given me by the earnestness and completeness of their coöperation. This work could not have been done without this superior assistance and coöperation. The length of the list, and the extent of the time over which the work has been in progress, preclude their individual mention.

I am also deeply indebted to several friends who have given me encouragement that has been exceedingly helpful, and who, by their deep interest and constant encouragement, have helped me to overcome obstacles that seemed very forbidding.

Volumes One and Two, herewith presented, are so interrelated and inseparable in context, being but different phases of the same problem, that they are treated as a unit and neither volume should be considered apart from its cross references to the other. Those who are familiar with the expense of illustrations, and particularly of four-color process engravings, will appreciate that no trouble and expense have been spared. The color separation negatives for the four-color histopathological plates were made by us directly from the tissue sections (not Lumière or Paget), which is, we believe, a distinct advantage over hand-colored photographs or drawings, all of which *introduce the personality of the artists.*

I wish to thank the printer and the various engravers for their splendid coöperation and assistance in presenting this message.

Weston A. Price.

8926 Euclid Avenue
Cleveland, Ohio
August, 1923

INTRODUCTION.

THE GENERAL STATUS OF HUMANITY AND THE HEALING PROFESSIONS.

Since a new truth is a new sense, because with it an individual can see things that he could not see before he had that new truth, and things that persons who have not that truth cannot see, it must follow that the blindness of ignorance is not only the greatest inconvenience but the greatest affliction to humanity. The tragic position in which our modern civilization finds itself with regard to dental infections and their local and systemic effects, is emphasized by comparison with the absence of similar suffering among many less civilized peoples, and it is entirely probable that the coming of many of the new comforts which have amounted to reformations in our methods of living, has exaggerated to a great extent our present conditions. There exists today, in the minds of the members of the laity as well as in those of the members of both the medical and dental professions, a confusion of ideas regarding dental infections that amounts to a group of misapprehensions and contradictions leading everywhere to uncertainty. We feel sure there is no other major affection about which there is this maze of uncertainty and apparent contradiction. The purpose of this volume and of the extended researches which it represents, has been pursued and inspired with the hope that it will aid by bringing some fundamental new truths which will furnish us all with an additional or new sense which we may term a *dental infection sense.*

In approaching this subject we should have in mind that dental disease is one of the most universal of all the afflictions of humanity. As has been emphasized, only a few isolated tribes or limited civilizations have been or are free from its curse. According to our statistics, over ninety per cent of the children in the United States have dental infection in some form. The statistics for the cause of absence and tardiness in school work show dental infections to be the chief factor, and these largely because of the immediate discomfort from dental caries. This, however, does not constitute the most serious phase of dental infections:

namely, their systemic expressions. I am more and more impressed and convinced after more than twenty-five years of intensive study of this problem, that the members of the healing professions have generally a quite incorrect conception of the variety and extent of the systemic expressions of dental infections, and this because of the absence of this new sense which is just developing with the coming of new, though meager truths.

Surely, the lay humanity is helpless to save itself, and, as with all the other scourges, so many of which have been removed by the coming of new senses through new truths, it is dependent upon the healing professions for relief and ultimate rescue. Unfortunately, many difficulties have combined to aggravate and complicate the already obscure problems. In the first place, the lack of coöperation between the medical and dental professions has been an incalculable hindrance and disadvantage to both the progress of healing science and the well-being of society. Much of the research that has been done on this problem has been by those who, by the very nature of things, have been handicapped by an opportunity to check every detail and check up against the clinical. The clinicians have had neither training nor time available to interpret their clinical findings in terms of laboratory procedure. The whole problem has been clouded by a group of contradictions of symptoms which, probably more than all other matters combined, has delayed progress. What could be more convincing to the medical and dental practitioners that dental infections do not have systemic expressions than to find that the majority of people examined with extensive dental infections, and some exceedingly so, have as yet no systemic disturbance; and the converse, that the people suffering severely from obscure disturbances, have relatively slight evidence of dental infection? If some of the new truths we are presenting in this volume are fundamental and correct, as we believe they are, they not only harmonize this apparent contradiction but suggest that these are just what we should expect.

The growing tendency for coöperation between the medical and dental professions, so long withheld, is a first requisite in humanity's behalf. However, until our dental colleges teach more of general medicine and clinical pathology, and the medical colleges teach more of dental pathology, both local and systemic, humanity must wait and suffer. The slow rate of progress of the past can only be accelerated by the perfection of organization and equipment for research in this field, a first requisite of which is the closely coöperating group of specialists working with such complete harmony that every step is interpreted in terms of all those factors which are held in common, as well as those which relate chiefly to the field of each specialist. To be more specific, the solving of these problems requires the skill and experience of each of the following: a well trained clinical dentist who knows every detail of the steps in the various operations and of the dental structures, physical, chemical, anatomical, and surgical, the histopathologist, biological chemist, general pathologist, serologist, and internist.

We cannot conceive of anything more monumental and personal than the responsibility of each and every member of the healing professions for the solution in humanity's behalf of this problem. The outstanding feature of the present moment is the utter meagerness of the effort that is being made to solve this problem in proportion to humanity's need. If we would compare this effort with that, say of farm stock or timber land, it is so insignificant as to be a cause for deep chagrin and humiliation, if not a consciousness of a misplaced trust on the part of humanity. This has been looked upon as a problem of dental research and, as such, has been left largely to the dental profession. Endowments have not been made available and the few workers in the dental profession who have had a vision of the responsibility and opportunity, have been completely handicapped by lack of moral and financial support. Their feeble strength has gone out in battering against a great wall of impenetrable difficulties ahead, while they have been flanked on each side by indifference and lack of equipment. This is one of humanity's greatest problems today and, as such, is worthy of the most splendid support, moral and financial, that can be given to any of its interests.

ANALYSIS OF PRESENT CONDITIONS.

THE GENERALLY ACCEPTED BASES FOR THE INTERPRETATION OF DENTAL INFECTIONS.

Each dental caries, dental abscess, gingival and alveolar inflammation and necrosis, has been interpreted as essentially infective processes, and hence their extent is essentially a measure of the infection. It now seems strange that we should have stumbled so long and interpreted the effect, as expressed in extent, as a measure of the cause. It has generally been accepted that the infection is produced by organisms presenting specific attacking powers for the dental and supporting tissues involved, and particularly in the case of gingival infections it has been looked upon as being largely a bacterial invasion, contracted by contamination with the involved organism. It has been anticipated, that the first step in the eradication or prevention of these diseases would, of necessity, be the identification of the specific causative variety or strain of organism, which would be followed by a suitable warfare against it. We have looked upon various individuals as comparable, and hence the effects produced by organisms as comparable. On these premises we have accepted a tentative set of rules of interpretation, formulated for, and applied to, all and various members of the human family. These rules, as generally accepted and applied, are about as follows:

1. Human beings are similar, and therefore comparable in their reactions to dental infections.
2. That dental infections, when they occur at the apices of roots, are produced by the invasion of that area by organisms from the mouth which enter that tissue through the open pulp canal; and that the question of danger from such an infection is dependent upon the invasive qualities of that organism.
3. That roentgenograms of teeth will reveal the presence of infection.
4. That infection will express itself as absorption.
5. That the apparent extent of the absorption is the extent of the infection.
6. That a given dental infection will express itself in the local tissues of the mouth approximately the same in all people.
7. That a tooth without visible absorption at its apex is not infected.
8. That a tooth with visible absorption at its apex is infected.
9. That pulps of teeth not exposed by caries are not infected.
10. That pulps of teeth with periodontoclasia pockets not involving the apex are not infected.
11. That an area of absorption, if present, can be disclosed by the roentgenogram.
12. That the quantity or extent of the absorption is a measure of the danger.
13. That flowing pus from a fistula is, necessarily, very dangerous to the patient.
14. That infected teeth can be sterilized readily by medication.
15. That usual medications do not injure the supporting structures.

16. That root fillings fill pulp canals and continue to do so.

17. That even a poor root filling is better than none.

18. That so called modern dentistry is a great and unmixed blessing.

19. That the field of the dentist is the oral cavity.

20. That a dentist or physician, and especially experts, can look at roentgenograms of the teeth and diagnose what should be done for the patient.

21. That local comfort and efficiency of treated teeth are an evidence and measure of the success of an operation.

22. That when infected teeth produce disturbances in other parts of the body, it is primarily because the patient is overwhelmed by a large quantity of infection.

23. That the quantity of infection in a tooth with a good root filling could not be sufficient to produce serious systemic disturbance, both because there is no place for bacteria and the quantity would have to be large, even teacupfuls, since the germs in dental infections are understood to have exceedingly low virulence or disease-producing power.

24. That there is adequate information available to practice dentistry properly and safely.

ARE CONDITIONS SATISFIED BY THESE OLD AND CURRENT INTERPRETATIONS?

According to the accepted fundamentals as presented in the preceding paragraph, the individuals showing the most extensive areas of tissue absorption about dental infections should be considered to be the persons having the most serious ones; and, consequently, we should expect that our worst cases of systemic involvement would be found in this group. Notwithstanding the almost universal belief that this is so, as a matter of fact, when we tabulate after careful clinical examination, we do not find that the evidence substantiates this, for we find that the individuals with these extensive areas of absorption resulting from a given dental infection, not only frequently but generally, are the persons but slightly affected with systemic expressions during long periods of their lifetime. This seems like a paradox and has constituted one of the chief closed doors to progress in the interpretation of dental infections. Not only does the extent of bone change vary greatly in different individuals with a given amount of infection, but the type of bone change also distinctly varies with the same cause, so far as we can judge regarding kind and amount of dental infection. Again, the effect of treatment and the extent and permanency of improvement are not at all in harmony with the above accepted fundamentals; contrary to expectation, there is a wide variation in the morphology and biologic characteristics of the organisms producing each of the certain types of local tissue change and the distinct kinds of systemic disturbance. There are also group characteristics that are not satisfied by the preceding statement of fundamentals. These group characteristics are such that they cannot be harmonized or accounted for on the basis of environment, diet, race, etc.

GENERAL LINES OF INVESTIGATIONS SUGGESTED BY THE OLD AND ACCEPTED FUNDAMENTALS AND BY THE CLINICAL CONDITIONS FOR DETERMINING THE ROLE OF DENTAL INFECTIONS.

A careful review of medical and dental literature for the purpose of finding the origin of the accepted fundamentals and to ascertain whether they have been founded upon dependable observations, has demonstrated that they seem to have grown up much as Topsy did. They have crept into the literature and practice of the sciences and have been quite generally accepted, apparently without question. One of our first undertakings has been, therefore, to check over, as carefully as we might, to determine to what extent they were based upon fact. Consequently, an enormous amount of really constructive research has consisted in proving that certain accepted beliefs were not true. None, but those who have been so placed, can know the misfortune of being placed in the position of tearing down the foundations and being termed an iconoclast, about which hang some tragic chapters of dental history. It has, however, been necessary to build new foundations deep down into the substrata of physics, biology, and chemistry. We will not review in detail, for lack of space, a large volume of research work that has really been negative in result, in that it has only proved that the accepted theories were incorrect. In general, we have undertaken to determine to what extent teeth are infected and what the nature of that infection is; to what extent routine procedures have been efficient in eliminating dental infection; the efficiency of root-filling methods as applied from a physical and mechanical standpoint; the general biological laws underlying susceptibility to dental caries and to gingival infections; the local expressions of dental infections; the tendency to development of systemic expressions of dental infections; the biologic properties of the organisms involved; the acquired factors which modify these susceptibilities; the influence of each diet, environment, habits, altitude, physical and mental states, and age. This work has covered a period of over twenty-five years, during which we have used many hundreds of animals and have engaged the assistance of skilled bacteriologists, physicists, chemists, histopathologists, and serologists; and the deductions we are here making should be received as a preliminary report since we have not sufficient information, as yet, to make us certain that we are able to interpret correctly, and will expect to make additions and modifications as further information becomes available.

Some of humanity's unsatisfied conditions are the following:—

Why do some individuals tend so readily to have periodontoclasia, while others have practically no tendency to it?

Why does dental caries become a constant menace for some individuals, while others have practically no tendency to it?

Why is it that when teeth are extracted for some individuals the conditions found are so unlike those anticipated, as judged by symptoms and roentgenographic appearance?

Why do some individuals always have much trouble from the healing of the sockets after extraction, while others have none?

Why are tissues about some teeth so easy to infiltrate with anesthesia and others so extremely hard?

What is the so-called dry socket?

Why do some individuals react with so much depression following even minor surgical operations and react alarmingly from extensive operations, and how can they be anticipated?

Why are some cases of periodontoclasia and suppurative gingivitis and alveolitis so resistant to treatment and others so amenable?

Since some teeth have, because of conditions, an intrinsic value to the patient that is very great and since similar teeth may in some cases do harm that is very great, how can we determine with relative safety when they should be retained and when removed; or otherwise stated, how can we establish the factor of safety of a given patient in relation to a given tooth?

When do given dental operations constitute a potential harm to the patient and when a potential good?

How can dental diseases be prevented?

To what extent are degenerative diseases the direct effect and result of dental disease?

Why do organs and tissues cease to properly function and ultimately degenerate, thereby wrecking the whole life either by premature death or what is often worse, a long protracted and agonizing death?

Why is it that in about ninety per cent, as estimated by high authorities, the final blow is struck by an organism, usually the streptococcus, even in patients with such involvements as pneumonia, and where do the streptococci come from?

These are some of the questions that we have undertaken to answer in these volumes.

CHAPTER I.

CAPABILITIES AND LIMITATIONS OF THE ROENTGEN-RAYS.

PROBLEM: To what extent are the Roentgen-rays capable of disclosing dental infections?

INTRODUCTION.

Since it is not my intention in this volume to furnish an historical review and criticism of the literature on the many topics that will be presented, both because it would be beyond the scope of the presentation and because it would entail such a voluminous text that it would defeat the very purpose by its energy consuming detail and unwieldiness, I will, accordingly, make important references throughout the text without purporting to make an historical review.

I have selected for presenting as the first problem a study of the efficiency of the aid in dental diagnosis which is more depended upon by the members of both the medical and dental professions than any other—namely, the Roentgen-rays—and which, because of the almost implicit confidence of the members of the medical and dental professions, the members of the laity have come to look upon as being infallible and practically limitless in application. I have divided this first problem into three sections: (a) An analysis of the fundamental that *roentgenograms are capable of revealing the presence of infection;* (b) *That the apparent extent of the absorption is the extent and volume of the infection or focal area;* and (c) *That an area of absorption, if present, can be disclosed by roentgenograms.*

EXPERIMENTAL AND DISCUSSION.

A review of the literature of the past and present regarding the applications of the Roentgen-ray for the disclosing of dental infections, together with the accepted general practice of the medical and dental professions and the clearly defined attitude of the public, which has been trained by the medical and dental professions, establishes that it is so nearly universal that it must be

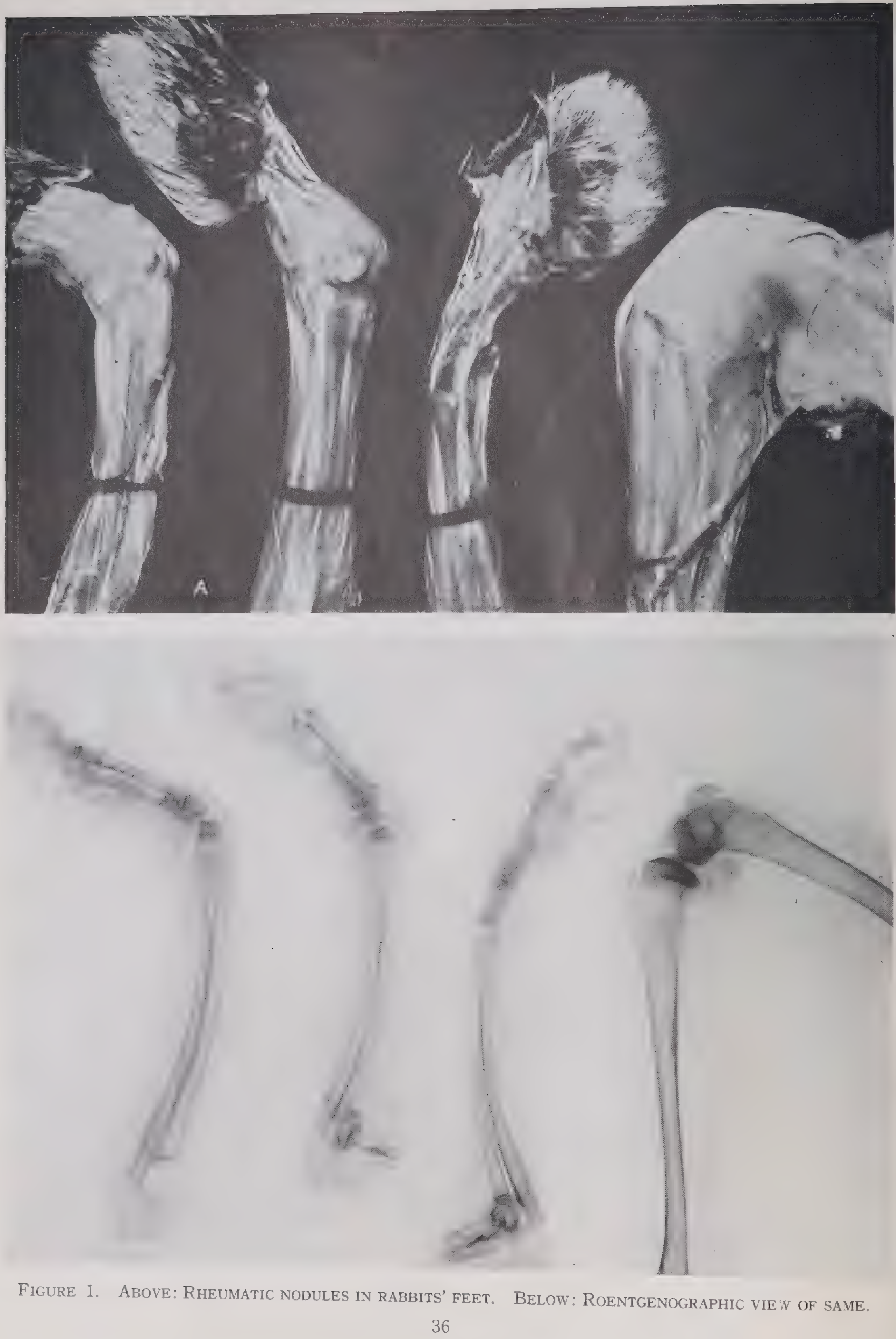

Figure 1. Above: Rheumatic nodules in rabbits' feet. Below: Roentgenographic view of same.

considered current belief, that the Roentgen-rays will reveal the presence of infection; particularly if present in bone, that the apparent extent is the actual extent of bone change; and that a chamber or area of lesser density, if present in soft or hard tissues, will, of necessity, be disclosed by the Roentgen-rays. No surer evidence would seem to be possible, establishing that this is the attitude of mind of members of the medical and dental professions and laity, than that the members of each continually bring roentgenograms of the teeth with the full confidence that the reading that will be made from the roentgenograms will answer the question as to what should or should not be done for that patient with regard to the teeth. An illustration of this attitude of mind is found in the current expression that the roentgenogram has made possible a living postmortem.

Our studies have included both the testing of the general principles on material that could be cut up and verified, and a careful comparison of the actual conditions as revealed at operation, with the apparent conditions as disclosed by the Roentgen-ray. It is, for example, common practice to have joints that are very badly swollen and with extensive involvements roentgenographed, in order that a proper diagnosis may be made for the patient. Figure 1 shows a photograph of three feet and one knee joint of a rabbit, each one containing extensive areas of infection. The three feet were much swollen, and on removing the skin little sacs filled with pus were present, in size and shape corresponding to garden peas. The knee, shown in A, was enlarged and dense with a pulsating mass of pus which involved the synovial membranes and joint capsule. B shows roentgenograms of these limbs; and the evidences of infection, as disclosed in the photograph, are not such as would be suggested by the roentgenograms.

Not succeeding in revealing the presence of pus in these cases, we selected two very extreme cases, as shown in Figure 2, where the quantity of pus present was so large that it was breaking out of the tissue. It will be seen that the Roentgen-ray does not reveal the presence or extent of these infections.

It is very true that we are dealing here with relatively soft tissue, the muscle, which, compared with the bone of the face,

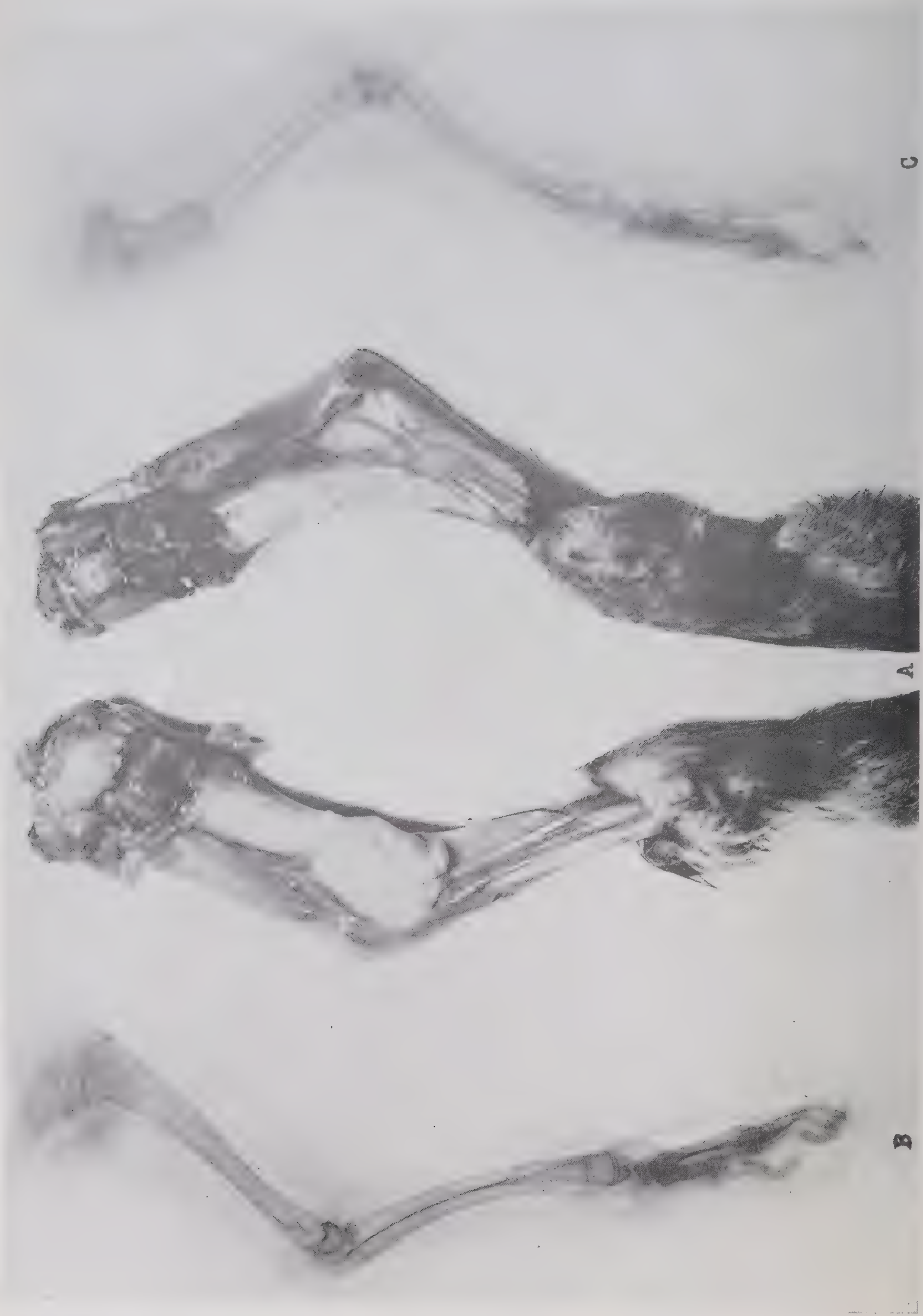

Figure 2. Very extensive purulent arthritis, which has extended beyond the joint capsules and between the muscles. Note: The roentgenogram fails to disclose the infection.

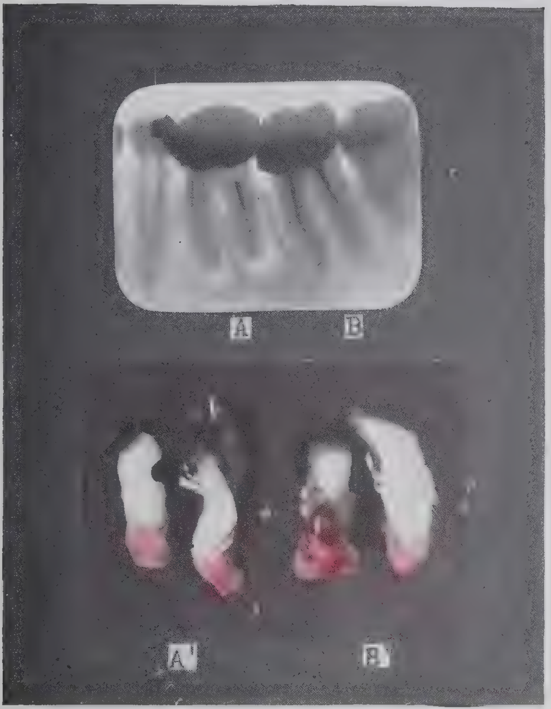

Figure 3. Comparison of the apparent with the actual. A and B show, roentgenographically, two maxillary molars. Note their difference. A′ shows the periapical granulomata attached to the roots of A, and B′ the periapical granulomata attached to the roots of B. The zones of rarefaction in A and B are obscured by zones of condensing osteitis.

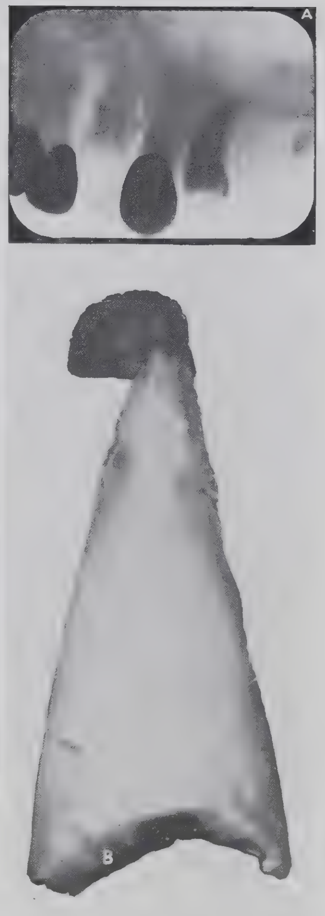

Figure 4. A, roentgenographic view of the root and apical area of a cuspid; B, an enlargement of the root and granuloma removed from this area.

may be considered to be very much less capable of differentiation, since the difference in density of pus and muscle tissue may be said to be less different than pus and bone. We have, accordingly, made careful comparisons of the apparent with the actual conditions as they obtain in the mouth. Figure 3 is a good illustration. In A and B, we have a sample of the usual roentgenographic disclosures. It is probable that not only the majority, but almost the complete personnel of the medical and dental professions and laity, would see in the first and second molars two radically different conditions of pathology. There is definite evidence of bone absorption about the apices of both roots of the first permanent molar, exceedingly little about the mesial root of the second molar, and practically none disclosed about the apex of the distal root of the second molar. A′ and B′ show the conditions of these roots when extracted, each having extensive adherent granulomata, which granulomata were larger on the second molar than the first, though they were not revealed by the roentgenogram; and the granulomata seen on the first molar were very much larger than the areas suggested by the roentgenogram. Our large accumulation of evidence of this type has crystallized our convictions into quite definite form, as expressed in succeeding chapters.

Figure 4 is another illustration. The root shown between the two gold crowns in A does not appear to have a granuloma; and yet, in B, it is demonstrated that this root when extracted had, notwithstanding its appearance in the roentgenogram, a very large granuloma. It may be argued by some that, if roentgenograms were taken from other directions or with rays having other degrees of penetration, these would be disclosed. Figure 5 shows an effort to disclose the presence or extent of pockets of periodontoclasia about a tooth. A and B show two different angles; yet neither the presence nor extent of the gingival and periodontal infection is definitely established. In C, some flexible gutta-percha points were placed in the gingival pockets and roentgenographed, which quite readily disclose much additional information. D is a roentgenogram of the extracted tooth to show the difference in the density of the root surrounded by pus and the adjoining roots. It should be noted that not even the roentgenogram shown in C discloses the actual condition; for, at the time of removal of the tooth, it was revealed that there was a continuation of the pocket through into the antrum.

It is common practice to determine the efficiency of root fillings as they exist in the mouth by means of the Roentgen-ray, on the

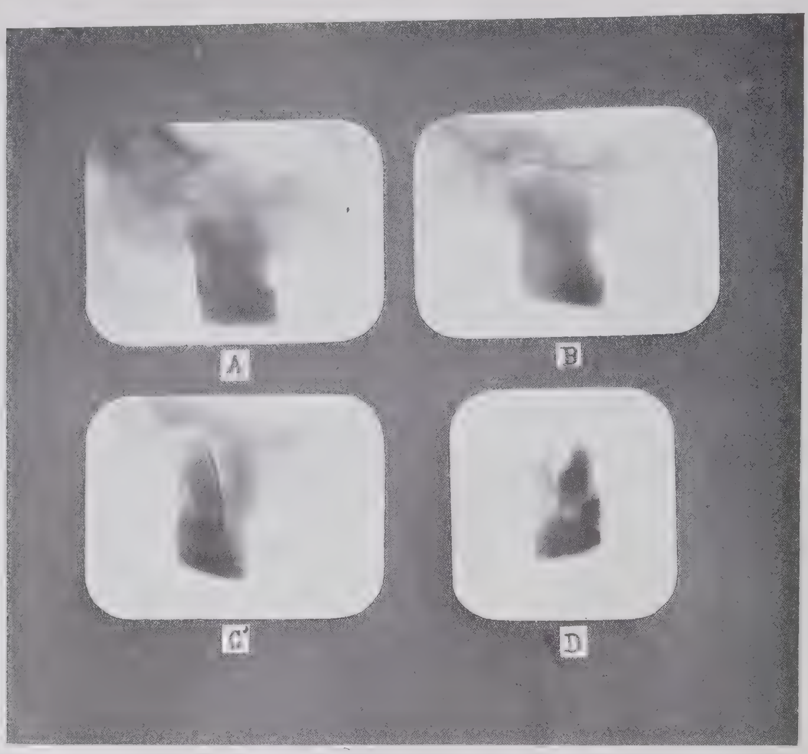

FIGURE 5. ROENTGENOGRAPHIC STUDIES OF PERIODONTOCLASIA: A AND B, DIFFERENT ANGLES; C, WITH FLEXIBLE GUTTA-PERCHA POINTS; D, EXTRACTED TOOTH.

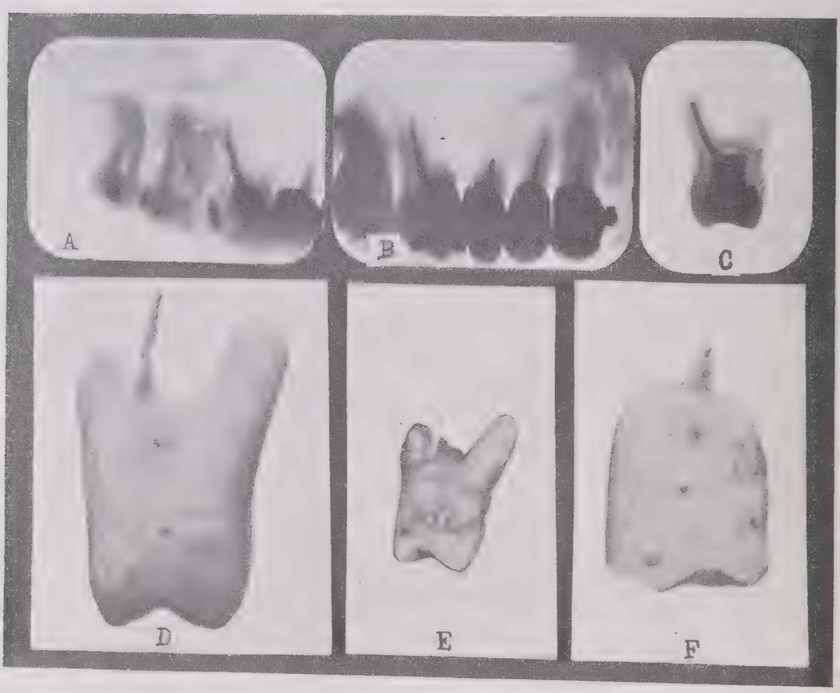

FIGURE 6. COMPARISON OF ROENTGENOGRAPHIC VIEW OF TEETH WITH THE PHOTOGRAPHS OF SAME WHEN EXTRACTED.

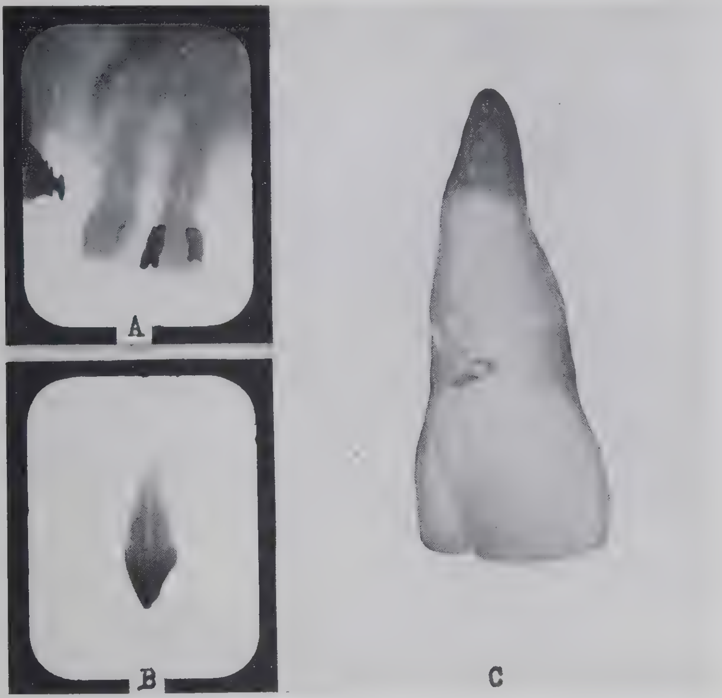

FIGURE 7. COMPARISON OF ROENTGENOGRAPHIC AND PHOTOGRAPHIC VIEWS OF AN INCISOR.

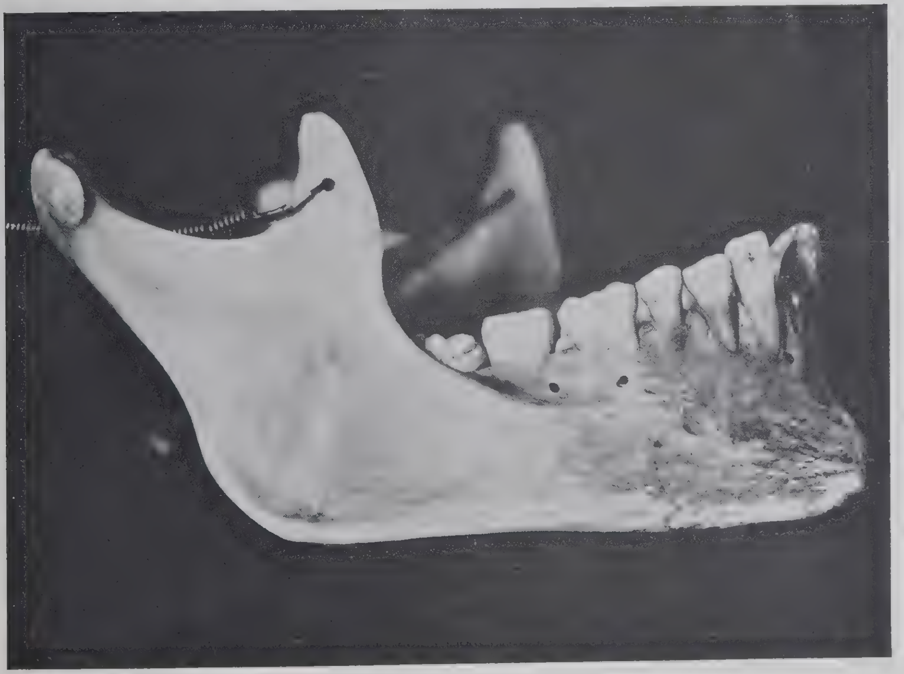

FIGURE 8. PHOTOGRAPHIC VIEW OF EXTERNAL OBLIQUE RIDGE OVER SECOND AND THIRD MOLARS, WHICH CAST THE SHADOW SHOWN IN FIGURE 9.

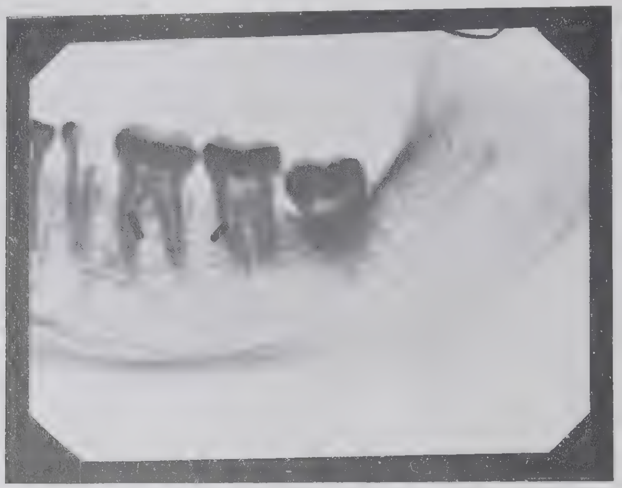

FIGURE 9 SHOWS A RADIOPAQUE AREA OVER ROOTS OF SECOND AND THIRD MOLARS. (SEE FIGURE 8.)

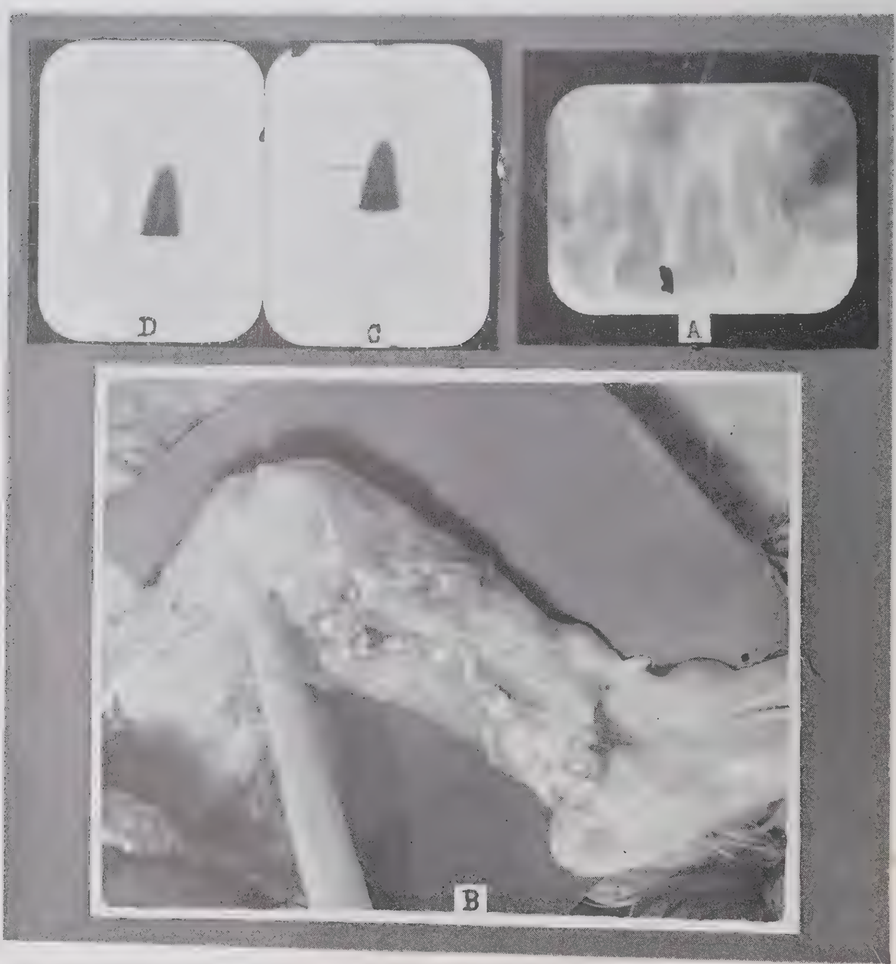

FIGURE 10. A ROENTGENOGRAPHICALLY INNOCENT TOOTH, BUT ACTUALLY A VERY DANGEROUS ONE.

presumption that the root filling is more opaque than the tooth structure, and being within the tooth structure, its true position and extent can be revealed by the Roentgen-ray. We have made many studies to determine this. A typical illustration will be seen in Figure 6, in which A and B show two different angles of the molars and bicuspids in a case under study. You will note that there is little evidence of the actual condition revealed in this case. There was an extensive cyst over the bicuspid and molar, only slightly outlined in the roentgenogram. Its presence and nature were established by microscopic examination of aspirated material. D and E show different photographic views of the molar from which both buccal roots had been absorbed, and one of the root fillings is seen projecting and exhibits a condition which is not revealed by the Roentgen-ray. F shows a photographic view of the second bicuspid from which the apical third was absorbed and its root filling extending considerable distance beyond the tooth; and yet, in the roentgenograms there is no evidence of this condition. It would appear in both A and B that the root filling is short of the apex. This case is referred to again in the chapter on Dental Cysts.

Figure 7 shows in A, roentgenograms of two central incisors, neither of which was tender to percussion or had given evidence of sensitiveness, one of which did not respond to temperature change when a search was made for a cause for rheumatism. It had a putrescent pulp and a very serious periapical involvement, without evidence of same in the roentgenogram. C shows the apical third of this root from which the pericementum had been destroyed, apparently for years, so that it was greatly discolored; and yet, the lamina dura and bone adjacent to the alveolus were found to be in almost normal position though not in normal condition, notwithstanding it is not a condition that is revealed by the Roentgen-ray. This is discussed in the next chapter.

Figures 8 and 9 show a photograph and roentgenogram of a mandible to illustrate the influence of the external oblique ridge in superimposing a dense bone, (varying greatly in different individuals), over the apices of molar roots, which modifies in large measure the roentgenogram as shown but only in part accounts for the condition as seen in Figure 3. While Figures 8 and 9 illustrate the effect of an interposing dense bone, our studies show that frequently the interposing hard substance may be the

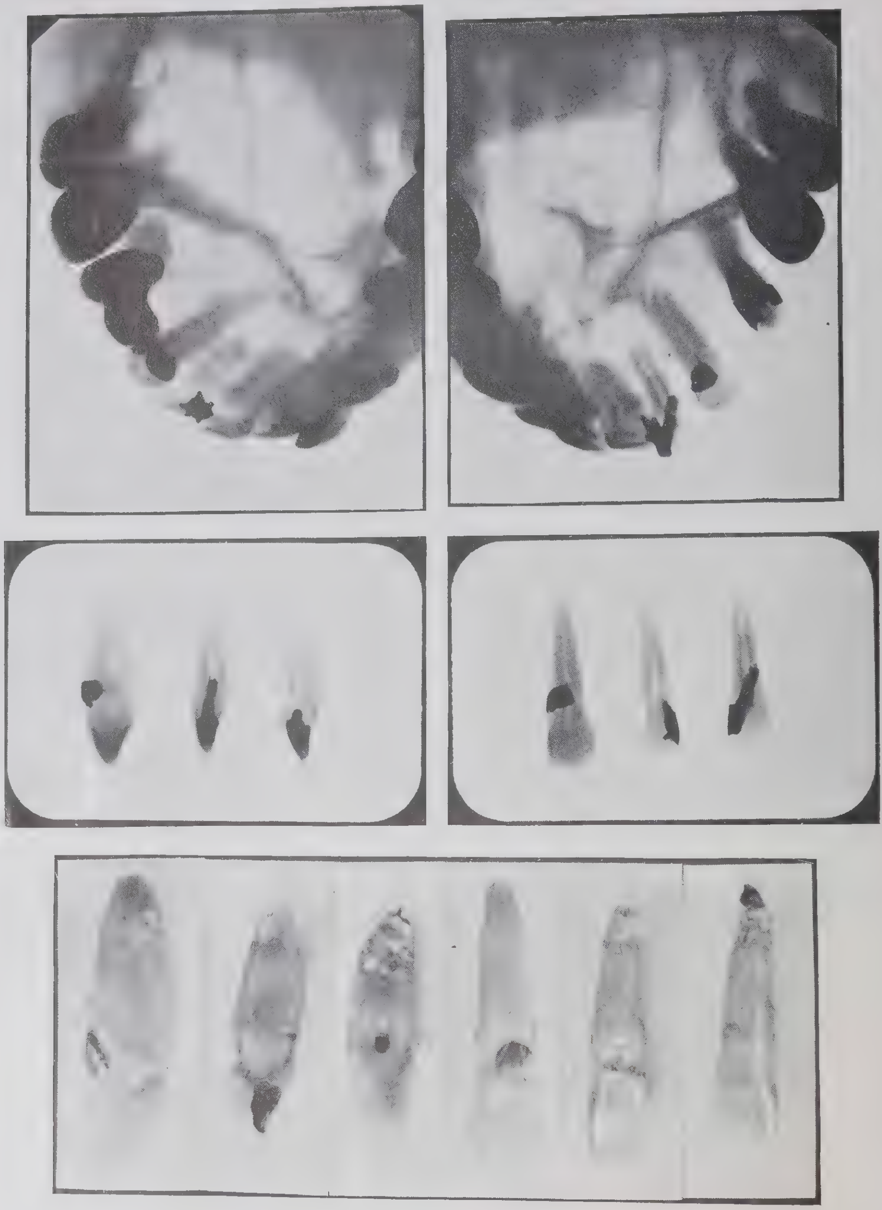

FIGURE 11. A COMPARISON OF THE ROENTGENOGRAPHIC AND PHOTOGRAPHIC STUDIES OF TEETH. NOTE THE ABSENCE OF EVIDENCE OF ACRETIONS IN THE ROENTGENOGRAMS OF THE TEETH *in situ* ABOVE, AND AFTER EXTRACTION IN THE CENTER, WHICH ARE VERY CLEARLY REVEALED IN THE PHOTOGRAPHS OF THE SAME AFTER EXTRACTION, SHOWN BELOW.

tooth itself, or another root of the same tooth, as illustrated in Figure 10, in which the roentgenogram of the central incisors is shown. There is exceedingly little difference in the condition disclosed about the apices of these two centrals; yet one is vital and the other non-vital, as disclosed in the search for a cause for a very acute and severe attack of rheumatism which had been recurring with increasing frequency and severity; and at this time, the patient could scarcely walk and was compelled to shuffle the feet along with almost no use of the feet and ankles. Thermal and electrical tests revealed the fact that the pulp was apparently non-vital in the central incisors showing the small filling. The color of both teeth was practically identical. The patient protested against losing the tooth. The reason for extraction and not root filling will develop in later chapters. The proof of local infection, secured for diagnosis, was established by aspirating from over the root and comparing the blood count with the patient's general circulation, which disclosed a higher leucocytic invasion than normal. The extraction of the tooth revealed a lateral canal with a small area of absorption at about the junction of the middle and apical thirds, which, being situated on the external surface of the root, was in line with the tooth and therefore not disclosed by the Roentgen-rays. The opaque tooth hid the area of absorption which was very slight. This is shown in C with a metal point placed in the lateral foramen. B of this figure shows a knee and ankle very profusely bathed in pus coming from the synovial sacs of the knee and ankle joints of a rabbit which was inoculated with the culture from this supposedly normal and harmless tooth.

It is quite remarkable how little difference the Roentgen-rays will reveal in the structure of a vital and non-vital tooth. Nor do we look for a change in the tooth structure as a rule. The change is expected to be in the supporting alveolar bone. Many teeth, however, carry depositions and incrustations, or zones of absorption, without any evidence of the same in the roentgenogram. An illustration of this will be found in Figure 11 which shows different views of a cuspid and two laterals by each method, roentgenographing and photographing, the latter both before and after extraction. The corresponding photographic views of the extracted teeth are shown in both photographs and roentgenograms. There is little suggestion in the roentgenograms of the extensive structural changes which are disclosed in the photographs.

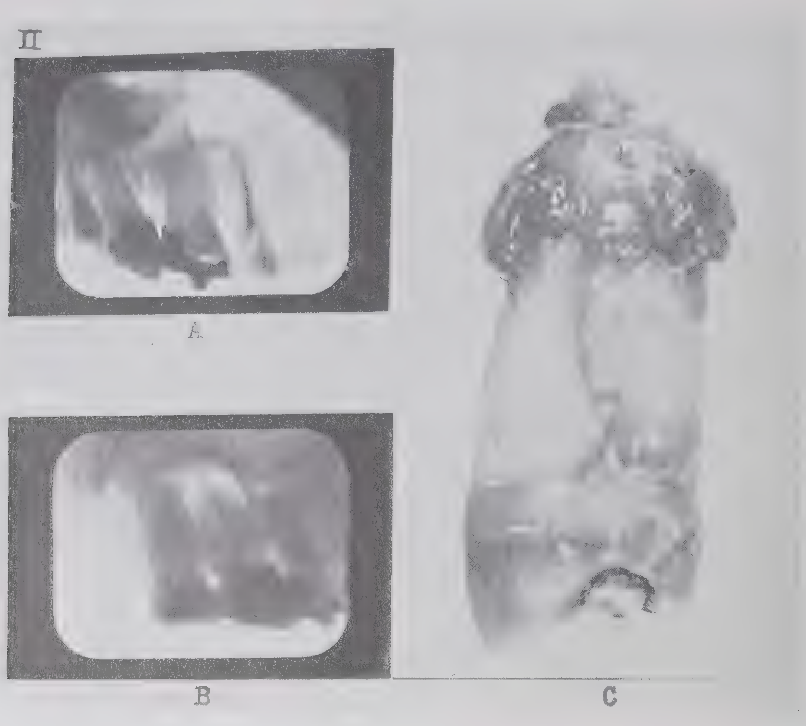

Figure 12. A, a high angle view of the upper molars. B, a low angle. C, the appearance of the extracted tooth.

One of the most common defects met with is the securing of roentgenograms of the upper molars because of the anatomical complications. The hard palate is often too low to permit the film to be placed laterally to the tooth, thereby requiring it to be placed at an angle if the apices of the roots are to be secured. While this condition can be partly overcome by retaining the lateral parallel position, there is a distinct limitation which requires the angle of incidence of the rays to be raised, which condition brings the malar bone into the field. This frequently casts a shadow of opacity, partially or entirely masking the details of the bony structure about the apices. Such a case is shown in Figure 12. In this instance A shows a roentgenogram brought by the patient from an excellent radiographer who, working with a group who had been looking for a cause for a neuritis in this patient, advised her that there was no contributing involvement of the teeth. B shows a different angle of these molars, disclosing a distinct area of radiolucency about the apices of the second molar. C shows an enlarged view of this tooth with its very extensive granulomatous mass, which evidences the possibility of

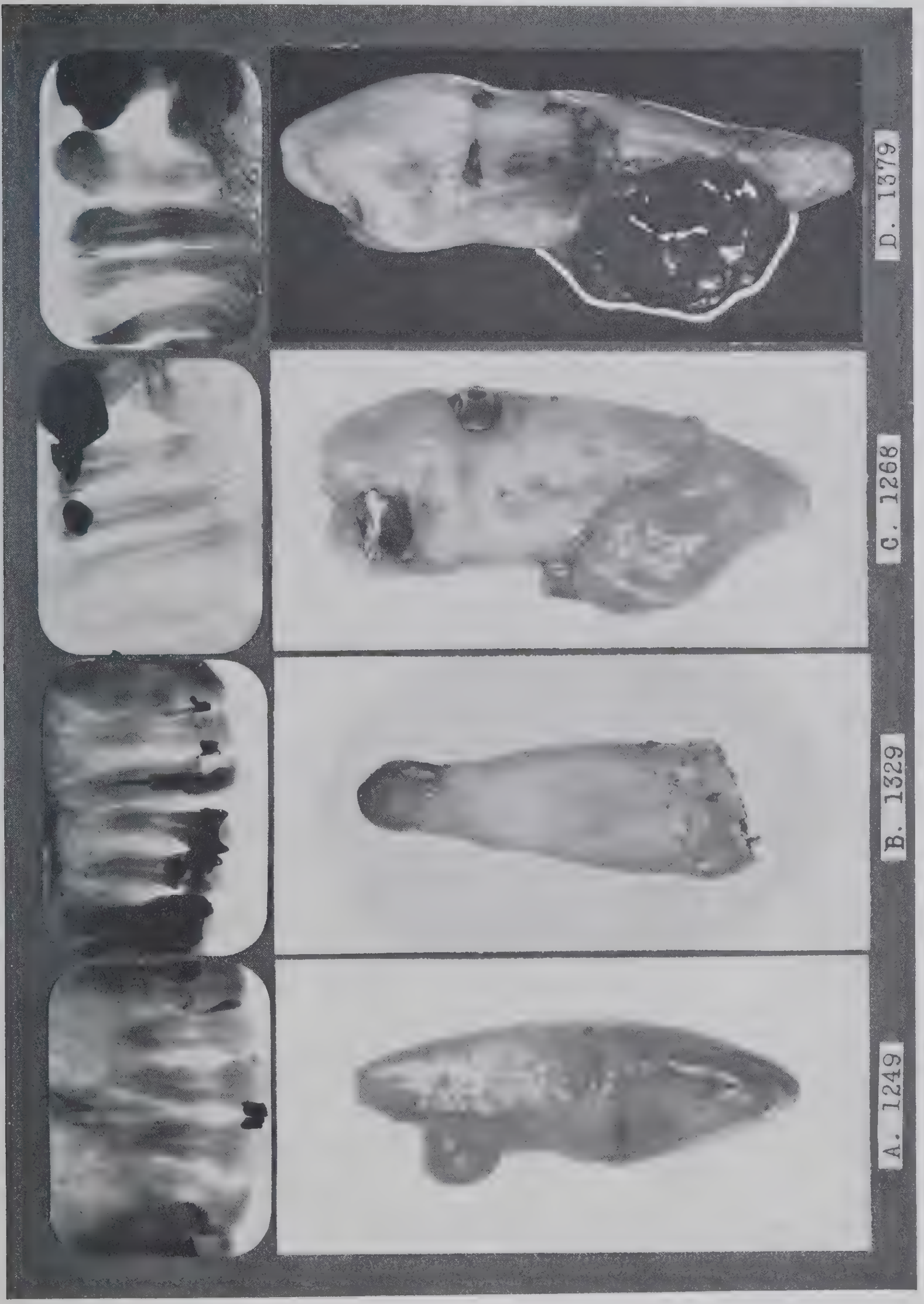

FIGURE 13. COMPARISON OF THE ROENTGENOGRAPHIC AND PHOTOGRAPHIC APPEARANCES OF EXTRACTED TEETH.

there being an extensive involvement of periapical tissue without its being disclosed by the Roentgen-ray.

It is not an uncommon condition for the largest of the multiple foramina of the tooth to be on the side of the root at any point, often about half way between the apex and the gingiva. In these cases there may be an extensive zone of rarefaction laterally to the root, which, because of the physical conditions, cannot be disclosed by the Roentgen-ray. Two of such cases are shown in Figure 13 in A and D. In D, the roentgenogram is shown above the tooth, and the photograph of the tooth shows the large granulomatous mass attached to the root. But this condition is more frequently found on incisors; and if the lateral foramen chances to be either labially or lingually from the pulp, instead of mesially or distally, neither the foramen nor the granulomatous mass forming about its exit will be revealed. Such a condition is shown in Figure 13-A. In this case the patient was suffering from acute rheumatism, and the examination of his teeth, roentgenographically, did not disclose this condition, which we have shown elsewhere to be significant from cultural and animal inoculation tests. The chamber of rarefaction was present but could not be disclosed, owing to its position, it being in the path of the root, which prevented the Roentgen-rays from disclosing it. Much as a dog would not be seen when it was lying behind a tree, except that in the roentgenographic work the obstruction of the tree is as complete whether the zone of rarefaction is between the tooth and the foramen, or between the tooth and the source of Roentgen-ray.

In Figure 13-B we have an illustration of the difference in the size of the area of rarefaction occupied by the granuloma, and its apparent size in the roentgenogram. I do not mean that this picture of the granuloma corresponds with the picture as shown in the roentgenogram, for in the former the tooth and granuloma are purposely enlarged. By making the proper correction for this change in size of the tooth, these still do not have the expected evidence in the roentgenogram. This is the more striking since the granuloma, as shown, is in relatively correct size, having shrunken considerably, due to exposure to the air, between the time of its extraction and its being photographed. This condition is a very common one which we will discuss later in the relationships between condensing osteitis and rarefying osteitis.

In Figure 13-C we have a condition somewhat similar to that in D; and while it is from a case of extensive periodontoclasia, its structural relationship to the tooth to which it is so closely adherent with a distinct separation from the surrounding connective tissues, except through the peridental membrane, only a small portion of which has remained vital, strongly suggests that this granulomatous mass is directly related to the tooth and products coming from it.

In Figure 14, I have undertaken to show a group of such conditions, with the teeth shown approximately normal size for comparison with the roentgenograms; and it will be noted that there is very little evidence of the existence of the extensive periapical absorptions such as are necessary to accommodate the large granulomata present. Indeed, it will in many of them be difficult without experience to determine which tooth in the roentgenogram is the one involved. In A, it is the first biscuspid; in B, it is the first molar; in C, it is the lateral; in D, it is the third molar; and in E, it is the second molar.

Since the roentgenogram is only a shadow, the angles of incidence of the rays to both the tooth and the photographic plate receiving the impression, have all significance. We are all familiar with the increasing length of our statures as we walk away from the sun in the evening, or the shortening of our shadow toward noonday; and, indeed, the length of this shadow has constituted one of the most important means for reckoning time, since the height of the object causing the sun's shadow was known, or could be determined. But in this field we find ourselves reversing the process and undertaking to determine the length of the object causing the shadow, all of which can, of course, be accurately done only when we know these angles of incidence. This is illustrated in Figure 15, in which I have shown three photographic views of the same tooth, which is an upper biscuspid and has a protruding root filling. In the first view from the left, the relation of the root filling to the apex is shown laterally, which is the mesiodistal position. When the same tooth is viewed from the buccal position, some of the root filling is covered because of the fact that it does not leave the root at the most dependent point; and since it is between the extension of the root and the source of ray, the shadow of part of the exposed root filling is obstructed by the lingual aspect of this root. But this view is taken at nearly right angles to the long axis of the root, a position that is impossible in this patient's mouth because of the low palate; and when the tube is raised sufficiently to have the shadow of the tooth fall upon a film that could be placed in the mouth, so much of the

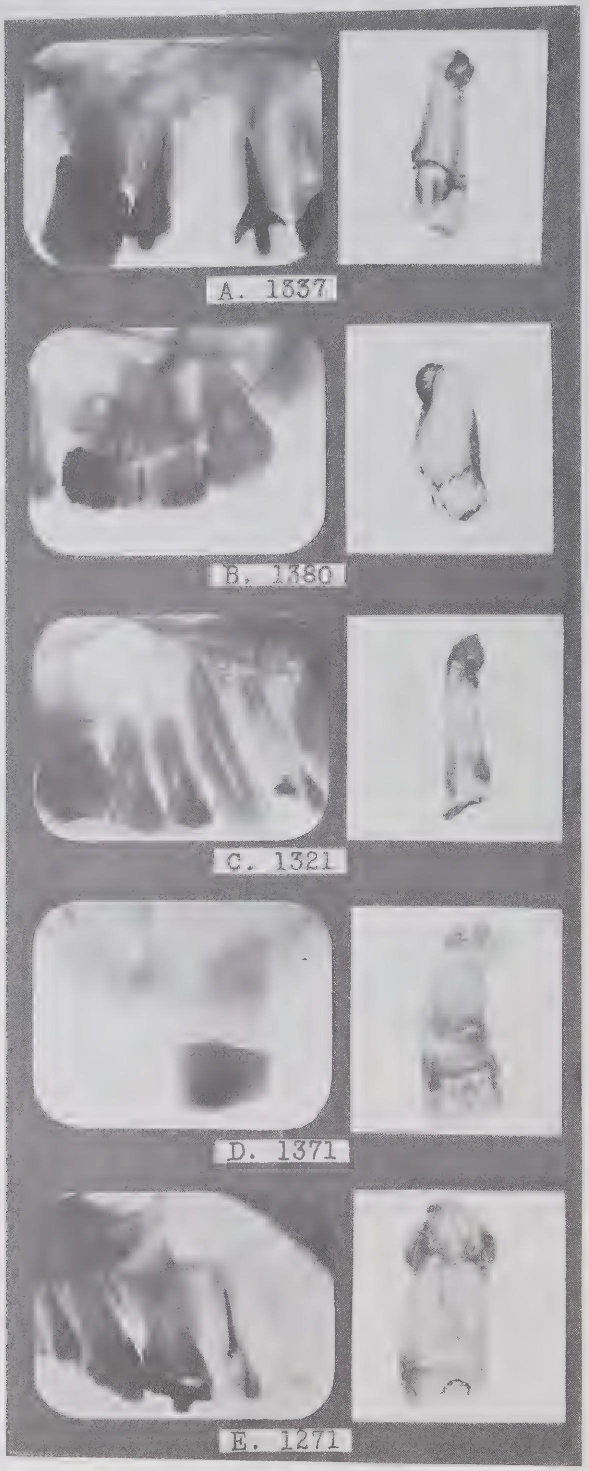

Figure 14. Comparison of the roentgenographic and photographic appearances of extracted teeth.

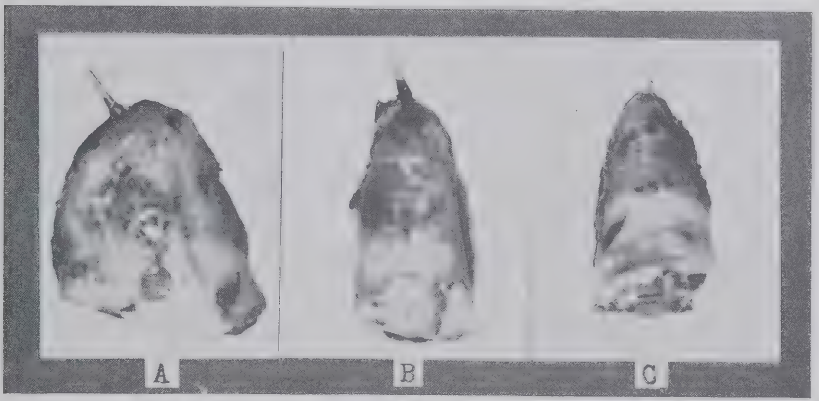

FIGURE 15. DIFFERENT VIEWS OF THE BICUSPID ROOT SHOWN IN FIGURE 6. A, SIDE VIEW, RIGHT ANGLE; B, LATERAL VIEW, RIGHT ANGLE; C, LATERAL VIEW, FORTY-FIVE DEGREES.

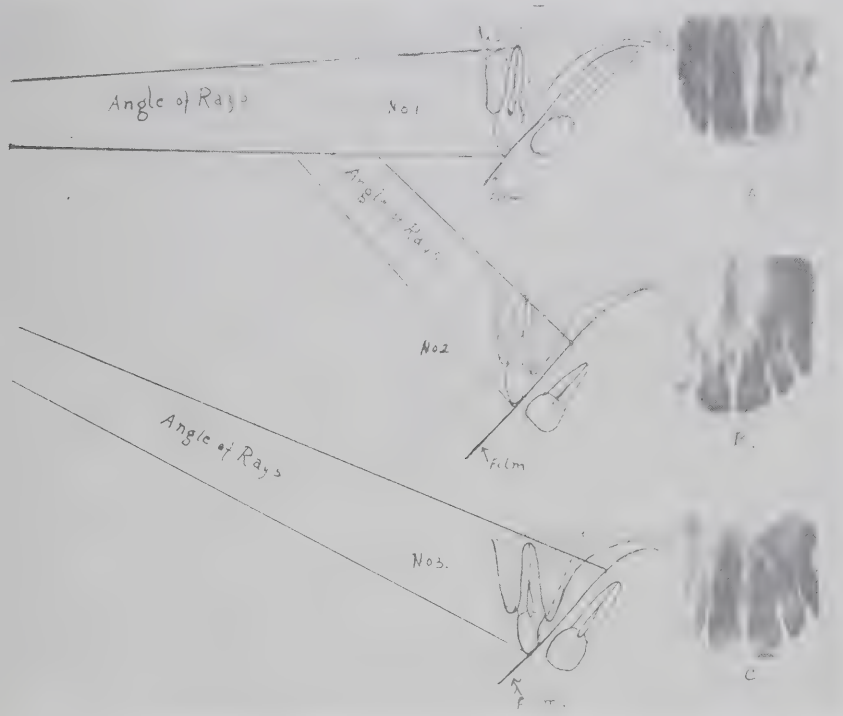

FIGURE 16. RELATION OF ANGLE OF INCIDENCE OF RAYS TO TOOTH AND FILM PLANES: NO. 1 AT RIGHT ANGLE TO PLANE OF TOOTH; NO. 2 AT RIGHT ANGLE TO PLANE OF FILM; NO. 3 AT RIGHT ANGLE TO A PLANE HALF WAY BETWEEN PLANE OF FILM AND PLANE OF TOOTH, THE CORRECT POSITION TO MAKE TOOTH APPEAR THE PROPER LENGTH.

exposed root filling is in line with the lingual aspect of this root, that it gives the appearance of only a short perforation. This is shown in the view to the right, Figure 15. Unfortunately, this is not an uncommon or unusual condition, for it is one that obtains very frequently.

I have published, previously,[1] an article on the relationship between the angle of incidence of the rays and the apparent size of the shadow. In Figure 16, I have reproduced this drawing and the roentgenograms that were used originally to illustrate it. In A it will be seen that a low angle of the ray at right angles to the long axis of the tooth, but with the plane of the film placed at an oblique angle to the plane of the axis of the tooth, makes an elongated shadow of the root of the tooth, illustrated in the roentgenogram also taken at this angle. B shows the same case photographed at an angle high enough to be at right angles to the plane of the film, in which case the tooth is foreshortened, as shown in the roentgenogram of the same case taken at this angle. C shows the correct position for obtaining the shadow of the tooth of the same total length as the length of the tooth, to obtain which the rays must fall at right angles to a plane which is half way between the plane of the tooth and root, and the plane of the film, as shown. C shows the roentgenographic appearance of the same case as A and B when so rayed.

SUMMARY AND CONCLUSIONS

From these few illustrations selected to demonstrate different conditions, it is apparent that the problem is not so simple as it is generally understood to be. While the analyses of the new problems disclosed by this study are made in detail in subsequent chapters, in general, it is demonstrated in these and a very large number of cases not included here, that the original premises a, b, and c, as stated, do not present the facts; and that these should be stated in the light of our present knowledge about as follows:

> **(a) That Roentgen-rays will not necessarily reveal the presence of infection, either in soft tissue or in hard; (b) That the apparent extent of the absorption is not necessarily the actual extent of the absorption; and hence, even assuming that the extent of the infection is the extent of the absorption, is not the extent of the infection; and (c) That an area of absorption may be present and not be disclosed by the roentgenogram, nor are conditions and relations necessarily as they appear to be.**

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[1] See bibliography.

CHAPTER II.

THE NATURE OF THE ORGANISMS INVOLVED.

PROBLEM: Is the danger from a dental infection primarily dependent upon the invasive quality of the organisms involved; or, otherwise stated, is it true that dental infections, when they occur at the apices of roots, are produced by the invasion of that area by organisms from the mouth which enter that tissue through the open pulp canal; and that the question of danger from such an infection is dependent upon the invasive qualities of that organism?

EXPERIMENTAL AND DISCUSSION

While many workers, besides ourselves, in the field of the bacteriology of dental infections, have called attention to the fact that streptococci are usually present in root end infections, it is generally understood by the members of the dental and medical professions that, whatever the classification of the organism, the injury it will produce has to do with the particular kind or strain of organism involved. Those most familiar with the literature are familiar with the fact that the organism involved is now generally understood to be a streptococcus.

The research herewith reported, which has covered many years, has centered about the following phases of the problem:

(a) What are the morphological characteristics of the organism?

(b) What are the biological characteristics of the organism?

(c) What is the relationship between the morphological and biological characteristics and their local and systemic tissue expressions?

(d) To what extent are the organisms influenced by variations in the pabulum, or culture medium, in which they grow?

(e) Are the organisms capable of producing specific toxic substances and, if so, under what conditions?

(A) WHAT ARE THE MORPHOLOGICAL CHARACTERISTICS OF THE ORGANISMS?

To determine these factors, we have made a study of the organisms secured from the various dental tissues involved, and have compared them with the strains recovered after their injection into various types of experimental animals. We have found, in general, that in approximately 98 per cent of instances, the dominating organism present appears as a coccus, growing in diploic and chain form, chiefly short chain; and that where the organism is taken from dental lesions, and inoculated into experimental animals and recovered from their tissues, in one series taken from forty different sources and inoculated into about one hundred animals, the organisms as recovered from two hundred lesions in those animals had the same morphology except that there was an increased tendency to grow in short chains and in diploic form until regrown in artificial media. In the histological sections of the tissues from these lesions, the organisms were seen almost entirely in diploic form. In later chapters I have discussed the teeth as carriers of infections for contagious and infective fevers.

In a large number of cases the culture injected, as grown from the original focus, contained in addition to this coccus other bacterial forms, chiefly a short bacillus and staphylococcus, also in spiral forms. In a few instances we recovered from tissues by cultural methods the staphylococcus as well as the diplococcus, and in less than 2 per cent staphylococcus only. As we now view this work, we do not feel sure that the diplococcus was not present in those cases where we did not identify it, having come to recognize that it is quite exacting in some instances regarding oxygen tension and hydrogen ion concentration; and where both organisms grew out, the diplococcus may have been overgrown. We do not question the presence of the staphylococcus, but we are not certain of the absence of the diplococcus. It is significant that animal passage generally destroyed all organisms except the diplococcus. Our recent methods of culturing are showing the presence of streptococci or diplo-steptococci as one or the only organism in infection of the tooth structure.

(B) WHAT ARE THE BIOLOGICAL QUALITIES OF THE ORGANISMS INVOLVED?

These have been determined by their reactions on culture media and animal tissues. We have found many varieties of the streptococcus. Figure 17 is made from sixty-seven successive cases and shows that many types of the streptococcus may be found in dental lesions, chiefly the following: fæcalis, ignavius, salivarius, infrequens, mitis, non-hæmolyticus I, non-hæmolyticus III, hæmolyticus I, subacidus, and pyogenes. The column marked "Per cent" shows the percentage of these various varieties occurring in the total number included in the study. The ratio or percentage of these to each other is expressed graphically by the solid lines to the left under "Graphic Expressions." This shows strikingly the very large percentage of fæcalis.

RELATIVE PREVALENCE OF DIFFERENT STRAINS

*Type of Streptococcus	%	Graphic Expressions
Fecalis	65½	
Ignavius	1½	
Salivarius	1½	
Infrequens	9	
Mitis	7½	
Non-Hemolyticus I	3	
Non-Hemolyticus III	3	
Hemolyticus I	3	
Subacidus	1½	
Pyogenes	4½	

* (Note—Streptococcus viridans is the group name of non-hemolyzing streptococci producing a narrow green zone when grown on blood agar)

FIGURE 17.

BACTERIAL CLASSIFICATION IN RELATION TO TISSUE AFFECTED.

Type of Lesion in Patient	S. Ignavius	S. Salivarius	S. Infrequens	S. Mitis	S. Non-Hemolyticus I	S. Non-Hemolyticus III	S. Hemolyticus I	S. Subacidus	S. Pyogenes	S. Fecalis	Percentage S. Fecalis	Ratio of Chance
Rheumatism			2		1	1				**7**	11	**7.1**
Heart										**2**	3	**1.3**
Nerves		1	3	4	2	1	2		3	**21**	33	**24.05**
Lassitude			2	1						**11**	17	**9.1**
Internal Organs		1	1	1						**8**	13	**7.1**
Special Tissues	1		3	1		3				**7**	11	**9.7**
No Lesions								1		**7**	11	**5.2**

FIGURE 18.

We have failed completely to establish a relationship between the various strains of streptococci and particular types of tissue lesions in the patient, and the results of animal inoculations have been similar, in that the particular types or strains of streptococci that were introduced, did not of necessity produce a particular type of lesion in animals, although various strains were found to reproduce in animals particular lesions possessed by the patient from whom they were taken. There was also no constant relationship between the biological properties, as expressed in sugar fermentations and the expressions in animal tissues.

(C) WHAT IS THE RELATIONSHIP BETWEEN THE MORPHOLOGICAL AND BIOLOGICAL CHARACTERISTICS AND THEIR LOCAL AND SYSTEMIC TISSUE EXPRESSIONS?

If, as has been so generally supposed, the particular type or strain of invading organism determined the tissue reaction and elective localization, we should expect that a careful study of the biological properties, such as sugar fermentation, would have a direct relationship to the type of tissue involved in a particular individual. To determine this we have made a careful study of the percentage of instances in which the various strains of the streptococcus were present, and have noted the particular type of tissue that was involved in that patient's body. The result of this study is strikingly shown in the chart in Figure No. 18. It will be seen, not only that the localization in the various structures is not limited to a particular type, but, on the contrary, the various tissues have been invaded indiscriminately by the different varieties of streptococcus. For example, the nerve tissues were invaded by all but two of the ten principal varieties of streptococci.

By expressing this relationship in percentage, we have an opportunity to compare the appearance of each of these varieties with its appearance on the basis of chance, assuming there was no localizing quality characteristic of each variety. This is shown for S. Fæcalis under the column, the second last to the right, entitled "Percentage S. Fæcalis." For this study a group of one hundred localizations was used; and hence, for any one tissue the total number of appearances of a particular variety, say Fæcalis, in proportion to the total number of appearances will give us the percentage. For example, in rheumatism there were 7 instances of Fæcalis out of a total of 63 appearances of Fæcalis. The percentage of appearances as rheumatism of Fæcalis was 11 per cent. The ratio of chance, were there no elective localization, would give on this basis 7.1; whereas, the actual appearance, as shown, was 7. For heart, the ratio of chance will give Fæcalis 1.3; the actual appearance was 2; for nerves, 24.05 and 21; for lassitude, 9.1 and 11; internal organs 7.1 and 8; special tissues 9.7 and 7; no lesions, 5.2 and 7. It will therefore be seen, that there is so close an adherence of the actual appearance to that which should be expected on the basis of chance, that we must conclude that the elective localization qualities are not dependent upon inherent biologic properties of the variety of the streptococcus involved. This is a matter of exceeding great importance since it shifts the burden of fundamental responsibility from the bacterium to the host, as will be clearly demonstrated later.

(D) TO WHAT EXTENT ARE THE ORGANISMS INFLUENCED BY VARIATIONS IN THE PABULUM, OR CULTURE MEDIUM, IN WHICH THEY GROW?

The next problem—namely, to what extent are the organisms influenced by the nature of the pabulum or culture medium in which they grow—must throw direct light upon this quality of accommodation of the organism. To determine this, several series of studies were made to ascertain the ability of streptococci to adapt themselves to their environment. These are shown graphically in Figures 19, 20, 21 and 22. For this study, strains were planted in a culture medium in which they were known to

FORMALIN

	1-160	1-320	1-640	1-1280	1-2560	1-5120	1-10,240	1-20,480	1-40,960	1-81,920	1-163,840	1-327,680
1-3	—	—	—	—	—	—	1+	4+	4+	4+	4+	4+
2-5	—	—	—	—	—	3+	4+	4+	4+	4+	4+	4+
2-6	—	—	—	—	—	4+	4+	4+	4+	4+	4+	4+
2-7	—	—	—	—	4+	4+	4+	4+	4+	4+	4+	4+
2-8	—	—	—	—	4+	4+	4+	+	+	+	+	+
2-9	—	—	—	—	4+	4+	4+	+	+	+	+	+
2-10	—	—	—	4+	4+	4+	4+	+	+	+	+	+
2-11	—	—	—	4+	+	+	+	+	+	+	+	+
2-13	—	—	2+	4+	+	+	+	+	+	+	+	+
2-17	—	—	4+	+	+	+	+	+	+	+	+	+
2-20	—	—	+	+	+	+	+	+	+	+	+	+
2-24	—	—	+	+	+	+	+	+	+	+	+	+
2-28	—	—	+	+	+	+	+	+	+	+	+	+
3-22	—	+	+	+	+	+	+					

+ = weak growth.
4+ = full growth.
— = negative growth.

FIGURE 19.

grow well, and to this medium, toxic substances were added to determine the point at which the toxicity would prevent the growth of the organisms. It was found that by taking the dilution just greater than would entirely inhibit the growth of the organism and maintaining the organisms in that concentration, they presently acquired a quality of growing quite readily in the presence of that poison; and by replanting, it was found that they would soon permit a new increase without seriously handicapping them. In this way, by slowly but continually increasing the concentration of the poison, it was found possible to grow streptococci taken from dental infections in one to three hundred twenty of formalin; whereas growth of this strain was inhibited by one to five thousand in its original strength. Similarly, it was found that these varieties would accommodate themselves to almost any irritant, even growing luxuriantly in twenty per cent alcohol (See Figure 21), one to ten iodoform saturated in alcohol (Figure 20), one to eight hundred phenol (Figure 22), one to two hundred thalium sulphate (Figure 22).

This has a very wide bearing upon our whole problem and suggests the answers to many questions. For example, we have often asked why it is that teeth that had been root-filled with iodoform, and in which the odor of iodoform was still persistent after years of time, would show an abundant growth of streptococci in the midst of the root dressing highly fragrant with iodoform. The organisms had very clearly accommodated themselves; for in our tests of feeding this chemical to streptococci, we found that they would ultimately grow in saturated aqueous solutions of iodoform.

Under another chapter we will discuss the reasons for the efficiency of iodoform in the treatment of wounds.

In our studies of the characteristics of the organisms growing in infected teeth, extending over several years, we have found that with an increased knowledge of the nature of the organisms and their power of accommodation and adaptation to their environment, they come to take on quite relatively stable, or well defined, characteristics, with regard to the kind of culture medium in which they will grow. With our increasing knowledge we are finding that the data accumulating show a quite definite per cent of teeth which are proven by positive culture to be infected, which means that whereas all positive cultures, of course, are positive, the absence of growth is not necessarily an evidence of the absence of an infection in the material

IODOFORM SATURATED IN ALCOHOL

	1-5	1-10	1-20	1-40	1-80	1-160	1-320	1-640	1-1280	1-2560	1-5120	1-10,240	1-20,480	1-40,960	1-81,920	1-163,840	1-327,680
2-28	—	—	—	—	+	+	+	+	+	+	+	+	+	+	+	+	+
3-22	—	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+

FIGURE 20.

ALCOHOL

	1-10	1-20	1-40	1-80	1-100	1-200	1-400	1-800	1-1600	1-3200	1-6400	1-12,800	1-25,600	1-51,200
48 hrs. 2-11 to 13	—	—	—	—	—	—	1+	4+	4+	4+	4+	4+	4+	4+
	—	—	—	—	—	—	4+	4+	4+	4+	4+	4+	4+	4+
2-24	—	—	—	—	—	4+	4+	+	+	+	+	+	+	+
2-28	—	—	—	—	4+	4+	4+	4+	4+					
3-1	—	—	+	+										
3-22	—	+	+	+										

— = negative growth
+ = weak growth
4+ = full growth

FIGURE 21.

PHENOL

	1-100	1-200	1-400	1-800	1-1600	1-3200	1-6400	1-12,800	1-25,600	1-51,200	1-102,400	1-204,800	1-409,600	1-819,200
2-1	—	—	—	—	—	—	—	—	—	+	+	+	+	+
48 hrs.														
2-15	—	—	—	—	—	—	+	+	+	+	+	+	+	+
2-17	—	—	—	—	+	+	+	+	+	+	+	+	+	+
2-24	—	—	—	2+	4+	4+	4+	4+						
2-27	—	—	—	4+	4+	4+	4+	4+						
THALIUM SULPHATE														
2-17	—	—	—	—	—	+	+	+	+	+	+	+	+	+
2-24	—	—	—	+	+	+	+	+						
2-27	—	—	—	+	+	+	+	+	+	+	+	+	+	+
3-22	—	+	+	+	+	+	+	+	+	+	+	+	+	+

— = negative growth.
+ = weak growth.
4+ = full growth.

FIGURE 22.

being cultured. When organisms grow in a root filled tooth for a long period of time, they tend to become anaerobic, and will frequently not start to grow in aerobic culture in less than from twenty to thirty days but will grow promptly under anaerobic or partial tension conditions. This has a very great bearing upon the procedures that have been advocated for the testing of teeth to determine when they are ready for root filling. Figure 23 illustrates this condition. Two tubes are shown which were inoculated at the same time from the old root filling material of a suspected tooth. The culture made aerobically remained sterile, whereas the culture made anaerobically grew out profusely in 48 hours, showing a good growth in 24 hours. In the illustration, the two tubes are supported in front of a white background, through the center of which passes a black strip. The clear transparent media of the aerobic culture shows the black of the strip through with nearly the same clearness that is seen on each side of the culture media, whereas the tube with the anaerobic culture, or rather partial tension in this case, for the organisms are growing in a medium covered with oil, which medium did not have its oxygen removed from it before inoculation, is sufficiently toxic to hide quite completely from view the black strip behind the tube. In subsequent chapters I have discussed the significance and importance of this in its various phases. When, however, these anaerobes are grown in a constantly increasing oxygen tension, they soon come to be aerobes, again illustrating this most important quality: namely, their capacity for accommodation to their environment.

(E) ARE THE ORGANISMS CAPABLE OF PRODUCING SPECIFIC TOXIC SUBSTANCES?

There has been practically nothing in the dental literature to throw light upon the complicated problem of the relative importance of bacterial invasion and the passage of the toxins produced by the organisms, to the tissues of the host. To determine this we have inoculated large numbers of animals with washed organisms and bacterial filtrates, using cultures from infected teeth of involved cases. The clinical symptoms will be discussed in succeeding chapters under special headings.

A typical illustration of the effect of the organisms upon the filtrate of the culture media in some cases, for all strains do not produce comparable toxins, is the following: A rabbit which was inoculated with 1 cc. of the filtrate from a culture grown

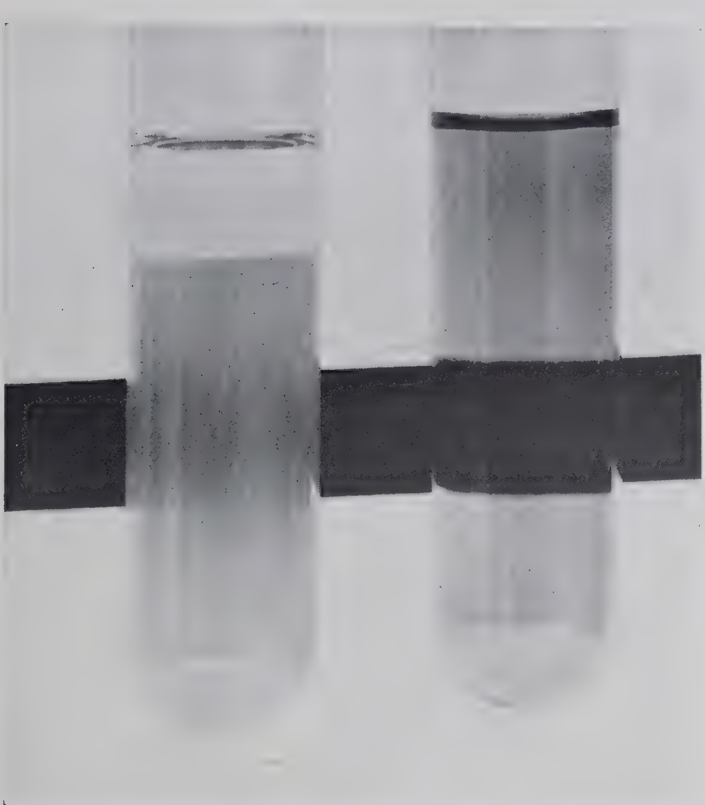


FIGURE 23. A COMPARISON OF THE AEROBIC AND ANAEROBIC GROWTHS OF INOCULATIONS WITH A STRAIN TAKEN FROM THE INTERIOR OF AN INFECTED TOOTH. AEROBIC, TO RIGHT, COMPLETELY TRANSPARENT, NO GROWTH; ANAEROBIC, TO LEFT, HEAVY GROWTH HIDING BLACK STRIP BEHIND TEST-TUBE.

from an infected tooth, died in sixteen days, having lost 35 per cent of its weight. On postmortem, it showed acute myocarditis, acute passive hyperemia of the liver and kidneys, and acute atrophy of muscles. The anatomical diagnosis for the cause of death was recorded as toxemia. We will review many instances later of animals dying from the effects of the toxin present in infected teeth, which teeth have been crushed and washed, and the washings filtered, the clear filtrate being inoculated into the animals, and producing quite as striking results as the above.

Similarly, the inoculation of animals with the washed organisms has demonstrated that very small quantities of these germs will be adequate in the case of many strains, to produce very serious structural changes with or without termination in death. Such a condition is illustrated in the following: Of 8 rabbits so inoculated, 2 died within 24 hours, 3 others within 9 days, and the other 3 within 13 days. The average loss of weight was 2.6 per cent per animal per day, as expressed in percentage of the total weight. The average loss of weight per animal before death was 18 per cent, or 203 grams. The average number of days lived was 7. Four of the 8 had a total loss of over 28 per cent, or an average of 319 grams. (*See Fig. 24.*)

There is a distinct difference, as is clearly shown, in the behavior of different strains which we have taken from infected teeth and cultured, then separated from the culture media and washed and suspended in sodium chloride. Of 15 rabbits so studied, none of which were included in the former group of 8, 4 gained in weight, an average of 336 grams, or an average of 26 per cent, nearly 1 per cent per day. The former group of 8 all died spontaneously as a result of their injections. None of this latter group died spontaneously, all being chloroformed. The other 11 of this group were chloroformed on an average of 10 days each, at which time they had lost on an average 10 per cent, or approximately 1 per cent per day. There was a wide variation in the amount of loss, one rabbit having lost only 1 per cent in 13 days, whereas, with another strain with which 3 rabbits were inoculated, they lost 17 per cent, each in 4 days, or an average of 4 per cent per day. In each of these groups, typical structural lesions were produced in various tissues and organs.

When we compare these effects of both the filtrates and the washed organisms on similar dosages of organisms plus filtrates, or rather the organisms in the culture medium in which they have grown without either filtering or washing, we have found that ½ to 1 cc. doses, which were usually given, produced quite different results in accordance with the particular strain being used. For example, in a group of 19 rabbits which had been so inoculated, and all of which were chloroformed, 7 proceeded to gain in weight, and 12 inoculated with other strains lost in weight. The average gain per rabbit in the 7 of this group was 88 grams in an average of 22 days, or an average of 4 grams per day. The other 12 inoculated with approximately the same quantities of other strains, lost an average of 11 per cent, or an average of 112 grams, in an average of 11 days, or 1 per cent per day. When we compare this part of the group with those of this group which died spontaneously, we find that on account of their more severe infections these 16 rabbits lost on an average, 18 per cent, or 209 grams in an average of 6 days, or 3 per cent per day, which it will be noted, is a much more rapid rate than in the preceding, and indicates a marked difference in pathogenicity of the strains.

In a larger series of a similar study, in which 108 rabbits were used, 55 died spontaneously in an average of 7 days, with an average loss of weight of 226 grams, or 20 per cent. This, it will be noted, amounted to a loss per day of 2.9 per cent per rabbit. Of this group of 108, 53 were chloroformed. Of these, 34 were chloroformed in an average of 23 days, having lost an average amount of 150 grams, or 11 per cent, or 1/2 of 1 per cent per day per rabbit. Nineteen of those chloroformed, in 46 days had gained an average of 167 grams, or 13 per cent, and 1/3 of 1 per cent gain per day per rabbit.

COMPARISON OF WASHED ORGANISMS AND WHOLE CULTURES.

No. in Group	Death	Days Lived	Loss			Gain		
			Actual	%	% per day	Actual	%	% per day
	A. Organisms Washed and Suspended in Sodium Chloride.							
8	*Spontaneous	7	203	18	**2.6**			
4	Chloroformed	31				336	26	.8
11	Chloroformed	10	119	10	1			
	B. Whole Culture							
7	Chloroformed	22				88	9	4
12	Chloroformed	11	112	11	1			
16	*Spontaneous	6	209	18	**3**			
55	*Spontaneous	7	226	20	**2.9**			
34	Chloroformed	23	150	11	.5			
19	Chloroformed	46				167	13	.3

* Spontaneous deaths in Group A—35%
* Spontaneous deaths in Group B—50%

FIGURE 24.

In all of these groups there were lesions in various organs and tissues of the body. We will not here discuss their nature and their relation to the disturbances from which the patients were suffering, as these will be taken up in subsequent chapters.

A typical illustration of the evidence that the host may build up and maintain a defensive mechanism by which the toxins are neutralized is found in the following experiment. A virulent strain which grew from an extracted tooth killed a number of rabbits in succession by the planting of the tooth beneath the skin, being thoroughly washed each time before replanting. The exudate aspirated from the vicinity of the tooth during the period while the animal was showing a vigorous defense, when injected through the skull of a rabbit into the brain, produced very much less disturbance than the same material aspirated when the rabbit's defense was rapidly breaking and it was nearly overcome by the infection. In fact, the filtrate from the material aspirated at the time the rabbit had a good defense, a fine Berkefeld filter being used, when injected into the brain of a rabbit, produced so little disturbance that both it and the control injected similarly with normal salt solution were as frisky as normals for weeks afterwards. And, similarly, an old culture that had become toxic by large quantities of dead organisms sufficient to inhibit its own growth, when injected into the brain of a rabbit, produced death in a few hours; whereas, the same quantity and approximately the the same bacterial density of a freshly grown culture similarly inoculated produced no evidence of effect for many hours. In the chapter on the mechanisms of defense I have discussed this question from another angle, and also in the chapter on sensitizations.

SUMMARY AND CONCLUSIONS

(a) With regard to the matter of morphology, we have found that in approximately 98 per cent of cases, the organism involved in root canal and root apex infection, a coccus growing in diploid and chain form, is present, and that this organism is nearly always the only one recovered from animal passage; and in some teeth this organism, though present, grows with very great difficulty; and we conclude that it is present in practically 100 per cent of cases, even where other organisms grow out in artificial medium and it does not.

(b) The biological qualities of the organisms growing in root end infections, as determined by their sugar fermentations, show ten varieties of diplococci present in one hundred cases.

(c) The elective localization qualities were found to be related neither to the morphology nor sugar fermentation qualities; that various tissues were invaded in the order of chance so far as the different varieties were concerned. Note: *This does not imply that the particular tissue breaking down is a matter of chance.*

(d) The organisms found in dental infections were found to have a very great power of accommodation to the influence of the culture medium, coming finally to grow readily in concentrations of poisons by which, originally, the strain was completely destroyed.

(e) The organisms growing in dental infections are found to produce toxic substances which have very far-reaching and disastrous effects on experimental animals.

We would, accordingly, summarize the role of the bacterial invasion in dental infection and express the fundamental involved therein as follows:

> **Dental infections involving root canals and their apices and supporting structures practically always contain streptococci, of which, biologically, there are many types or strains, any one of which may be the important causative factor for any of the various types of rheumatic group lesions, regardless of biological classification. The elective localization and attacking qualities are developed by the environment and are, consequently, a factor of the soil or host.**

CHAPTER III.

LOCAL ORAL STRUCTURAL CHANGES PRODUCED BY DENTAL INFECTIONS.

PROBLEM: Is there a constancy in the local oral expressions of similar dental infections?

INTRODUCTION.

It is practically universally expected and accepted that (a) *dental infection in bone will express itself as bone absorption,* and (b) *that similar dental infections will express themselves in the local tissues of the mouth approximately the same in all people.* This group of researches has been made to determine the correctness of these assumptions.

EXPERIMENTAL AND DISCUSSION.

We are dealing here with a matter that is so fundamental that to suggest even a possibility that it may not be true will be considered by many a gross presumption. This study has not been made to disprove but to verify, in order that a justification for our faith might be found, with the expectation that we would have to look elsewhere for the explanation for the gross confusion that exists. We have again two fundamental problems and two fundamental sources of information: Clinical material provided by the patients presenting different types of lesions and conditions, and researches on experimental animals.

To determine the various effects of infections on humans with regard to tissue reactions and their constancy in various people, we have only to study more intensively the clinical material that is available. That infected teeth have an area of absorption about them in proportion to the quantity and severity of the infection, will seem to be established by the examination of the available diagnostic reports made upon almost any set of dental roentgenograms.

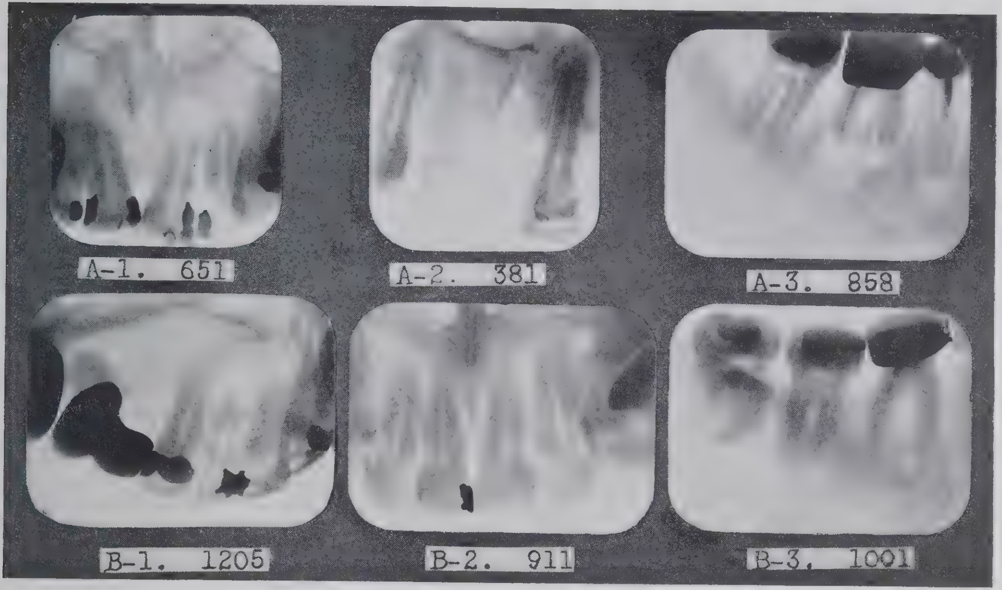


Figure 25. Illustrations of different types of reactions involving apices of roots and their supporting structures.

When we compare the roentgenograms made from similar conditions in a large number of individuals, we find, contrary to the presumption just made, very marked variations in the reactions from similar dental infections. Assuming that the amount of infection involved in the entire quantity of a putrescent pulp in either a central or lateral would be a similar and therefore comparable quantity to compare in another case, we have compared typical conditions as roentgenographically expressed and find such a condition as is illustrated in Figure 25. This shows in A-1 a right central for one patient and a right lateral for another in B-1, each showing very extensive areas of absorption. In A-2 and B-2 we show similar teeth from two other patients, which have comparable quantities of infection but which show almost no absorption about the apices. These are all of long standing and are typical of large groups of individuals.

It may be argued that the pulps of teeth may represent other factors and forces which we do not understand, and that therefore these conditions are not comparable as to quantity of infection, etc. We have, accordingly, added as A-3 a molar root and the

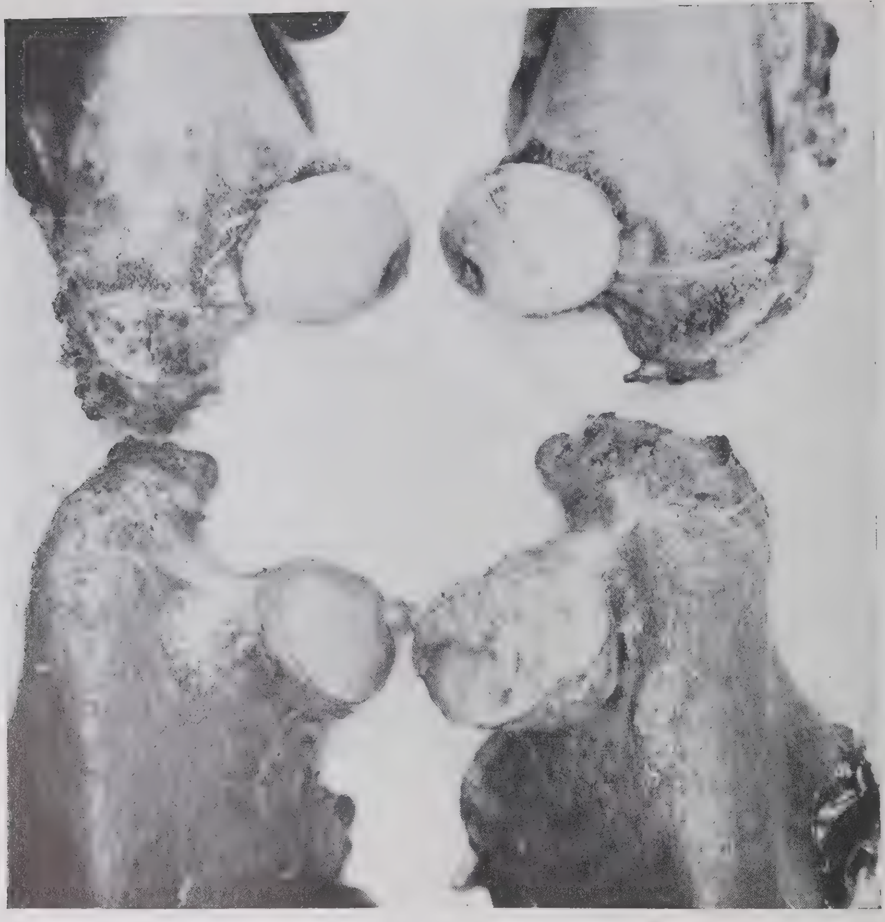


Figure 26. A degenerative arthritis of a rabbit's femur, with normal above.

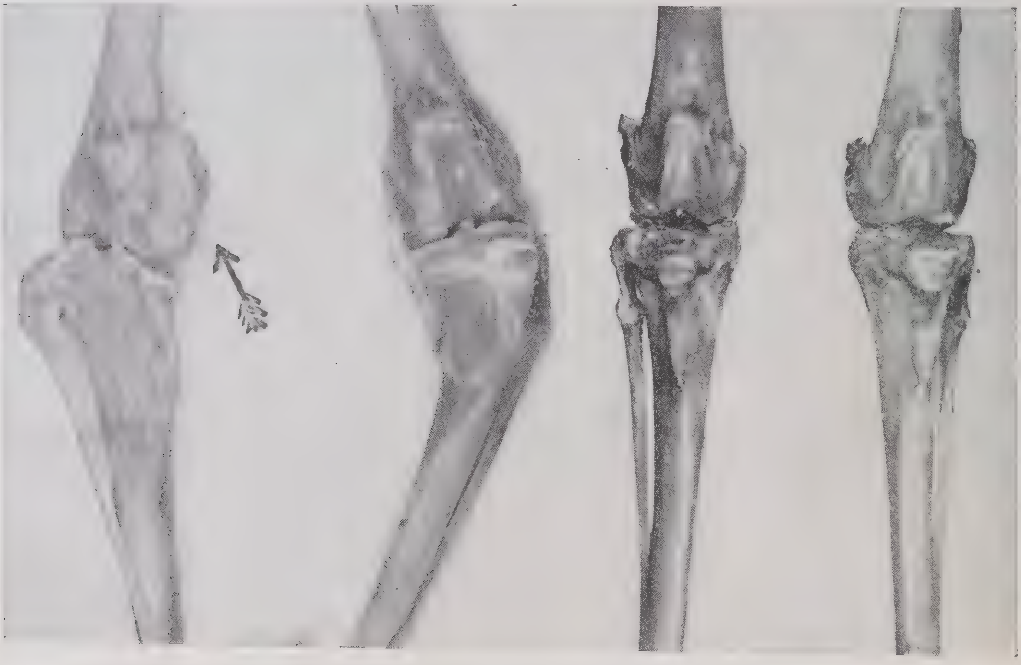


Figure 27. Proliferative arthritis of a rabbit's knees with normals to right.

structures beyond it showing very extensive absorption, in which one root is apparently nearly filled, the other partially so. In comparison with this we have shown in B-3 a molar tooth with apparently little or no root filling and a very little absorption about the mesial root and practically none about the distal root.

Culturally, practically all these pulp canals have been demonstrated to be infected by the same type of germ:—chiefly a diplococcus in fresh smear taken from the pulp chamber, but growing also in streptococcal form in liquid media. If, as has been quite universally accepted, all individuals react locally approximately the same, then the conditions found in A and B of Figure 25 will, of necessity, be related to the type of invading organism. The chart in Figure 18 of Chapter 2, Problem 2, "The Nature of the Organisms Involved," illustrated that no constancy has been apparent in the type of streptococcus found in different types of lesions. In the consecutive culturing of several thousand teeth from over a thousand individuals, which had been diagnosed as being infected, practically all were found to be so; and the type of tissue reaction found seemed clearly to be related to some factors other than the type of organism. The chart in Figure 17 of Chapter 2 shows graphically the relative number of different types of lesions produced by the different strains of streptococcus, and shows the relationship to be approximately that of chance and not dependent upon sugar fermentation qualities. If the difference in general structural change in Figure 25, A and B, is not due to the lesions being produced by different biological strains of streptococci, it immediately suggests that either various strains may take on the ability to produce these two different types of reactions, or these reactions may be related directly to differing qualities in the host.

Figures 26 and 27 show similarly two distinctly different types of reactions in the bones of rabbits. In Figure 26, we have extensive absorptions of the head of a femur, which is shown in comparison with its own mate of the opposite side, and two normals shown just above it. In Figure 27, the organism has produced an entirely different type of reaction; in this case, a deposition of lime salts instead of a rarefaction. Greatly enlarged knee joints are shown to the left and, for comparison, two normals shown beside them to the right. Since different rabbits inoculated with this culture produced the same type of reactions in bone tissue, we assume that the characteristic resided in the organism at this

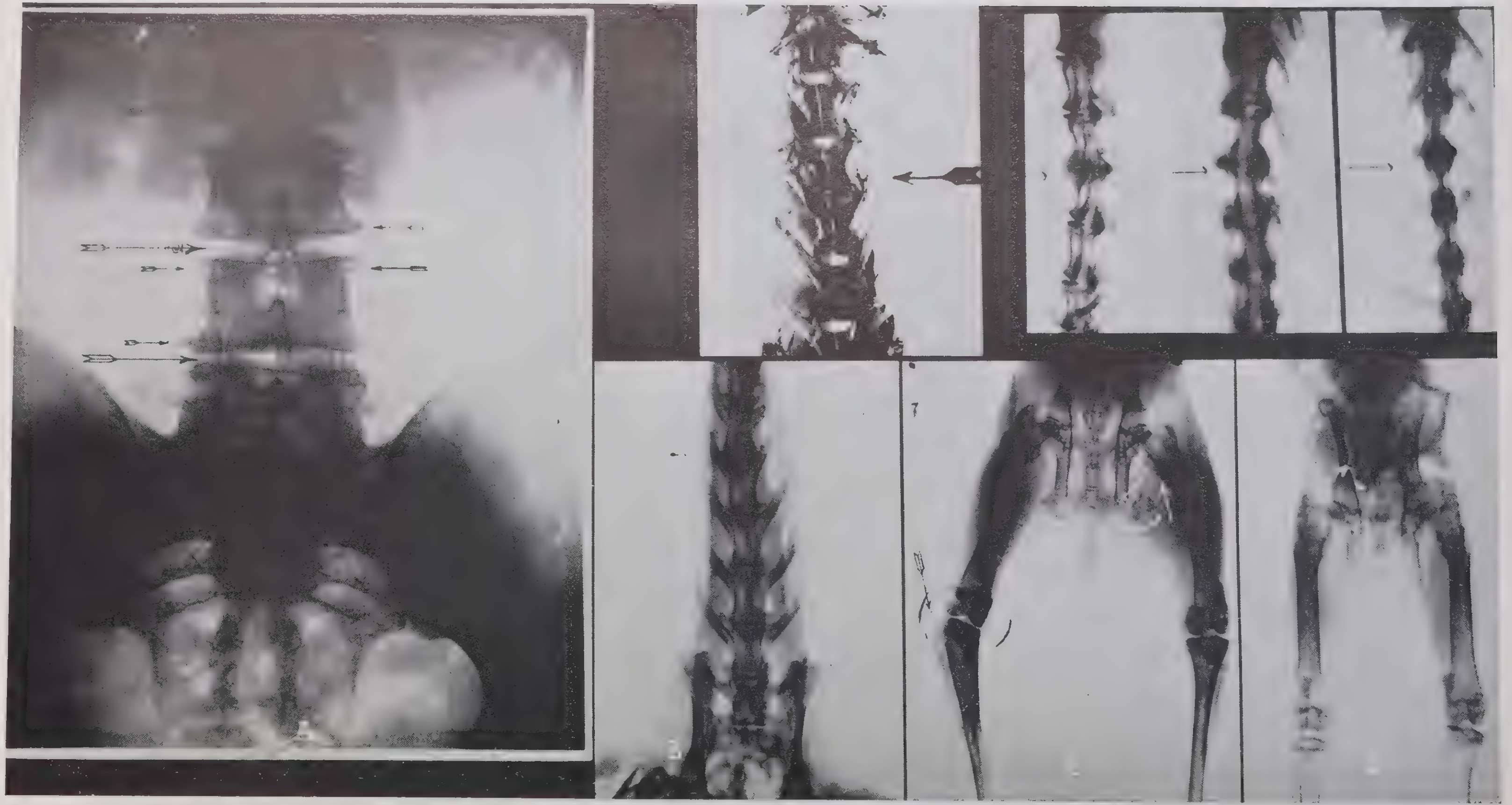


Figure 28. Proliferative deforming arthritis of patient's spine to the left. Proliferative deforming arthritis of rabbit's pelvic bones, knees, and spine, to the right.

time and not in the host. When we compare the reaction in the rabbit with the reaction in the patient from whom the organism was taken, we find that in the latter case it was from a man suffering from deforming arthritis, with such extensive depositions in his spine that he could scarcely bend or rotate from his head to his hips; and the roentgenogram of his spine, shown in Figure 28, and discussed in detail in Chapter 64 shows marked spinous production as do also the roentgenograms of the spines, bones, hips, etc., of the rabbits inoculated with that culture, shown also in the same figure. The source of the culture from which the inoculations were made producing the lesions shown in Figure 26, was a patient having marked nervous system disturbances without arthritis.

In Chapter 2, Problem 2, "The Nature of the Organisms," we have found that the qualities of the organisms, particularly that of growth, will be determined by the qualities of the culture medium, that they have the capacity to adapt themselves to their environment through a very wide range. This is also illustrated by the following: A strain which produced heart lesions in 93 per cent of a group of thirty rabbits inoculated with a twenty-four hour growth, produced heart lesions in only 10 per cent of rabbits when the organism was grown on artificial media for seventeen days.

Many of the researches reported in various chapters illustrate that, the organisms taken from different teeth of the same patient, produced when in the patient, similar local tissue changes, and when inoculated into rabbits produced similar types of bone change systemically to those suffered by the patient, as illustrated in Figures 27 and 28. These many studies suggest that the host determines in large measure the characteristics but not the biological type or classification of organism; and the nature of the tissue change which accompanies the presence of the organism and also determines that there is some difference, in most if not all patients, in the local tissue reactions related to the quantity of local infection, seems evident; but that the former is a direct measure of the latter, regardless of the characteristics of the host, is studied in the following experiments.

Results of these studies should be compared with the data developed in the researches presented in Chapter 2, "The Nature of the Organisms Involved."

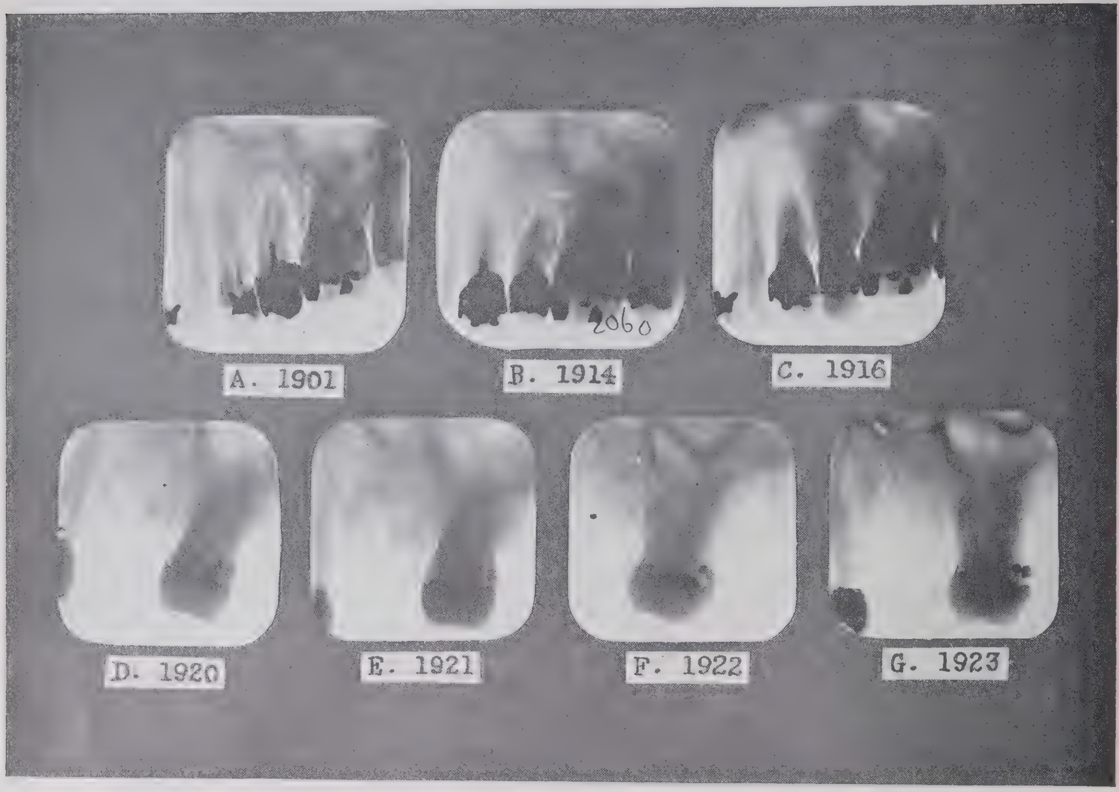


FIGURE 29. PROGRESSIVE VIEWS OF THE BONE ABOUT THE SECOND BICUSPID OF A PATIENT WITH DEFORMING ARTHRITIS OVER A PERIOD OF TWENTY-TWO YEARS. NOTE EXTENSIVE CONDENSING OSTEITIS IN C, DISPLACING RAREFYING OSTEITIS IN A, FOLLOWING TREATMENT AND REFILLING OF ROOT, WHICH CONDENSATION DISAPPEARED AFTER EXTRACTION. TOOTH AND BONE BOTH INFECTED.

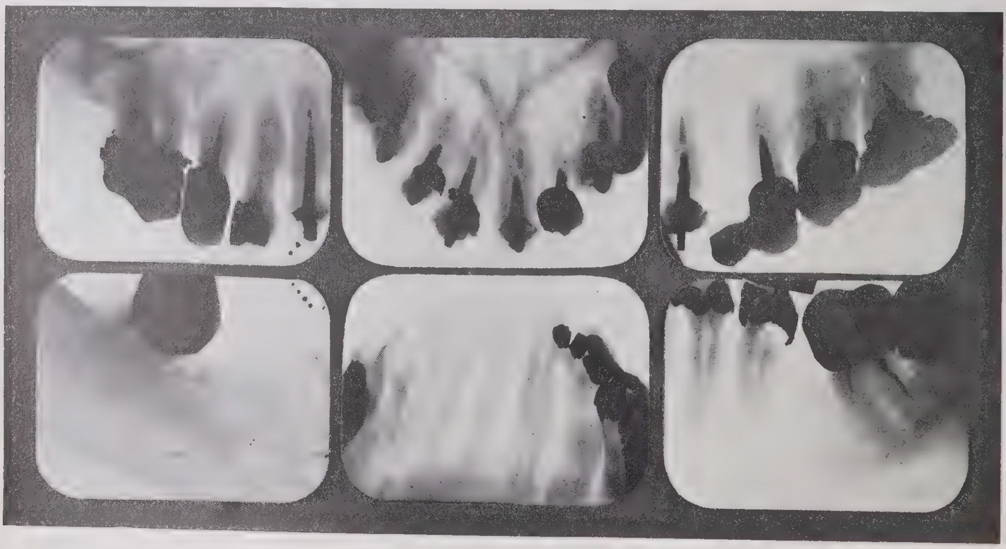


FIGURE 30. SHOWING SIMILAR LACK OF REACTION ABOUT SEVERAL INVOLVED TEETH OF SAME PATIENT.

Note: It will seem like a paradox or contradiction when I have said that the culture medium rather than the organism determines the type of tissue involved in the elective localization processes and then state that the lesions produced in the rabbits by the organisms tend under certain conditions to produce the same type of bone change in the rabbit as that organism would in the patient. In another chapter (Chapter No. 22) we show that the organisms rapidly lose their elective localization qualities when transferred to another type of media. This makes it necessary that the organism shall be transferred with as much dispatch as possible from the patient to the animal, and with as little modification by artificial growth as is possible.

Figure 29 shows the progressive history of a certain tooth: the upper right biscuspid. In 1901, twenty-two years ago, I made the roentgenogram shown as A, which was one of the early cases studied by this means. It shows clearly a tendency to a lessening of the density about the root apex. At this time I removed a poor and incomplete root filling; and after sterilizing the root with the regulation methods of the time, placed a new root filling with the assumption and confidence that all organisms had been destroyed and the tooth would remain in safe condition, for such was the confident teaching of the time. From time to time I made roentgenograms to determine that the bone was filling in about the apex. Six years ago I sent for the patient, having become convinced that it was not safe for her to have that tooth, notwithstanding the fact that it was apparently getting better, as proven according to the accepted fundamentals by the reconstruction of bone about the apex. In the meantime the patient had become progressively more seriously involved with rheumatic arthritis with so much rigidity that she had to be carried to the office. B of Figure 29 shows the dense bone forming about the apex. The tooth was not in the least tender. The tooth was extracted after using the actual cautery in the anesthetized gum at the neck of the tooth to destroy infection at the gingival border. It was cultured; animals were inoculated. The culture of the tooth showed a very profuse streptococcal infection. Cultures were taken from the bone surrounding the root apex to a distance of one-fourth inch from the apex, which grew out the same type of organism notwithstanding its density. About four months later, the same bone was cultured by sterilizing the external alveolar tissue with a cautery, after anesthetizing, and going through into the alveo-

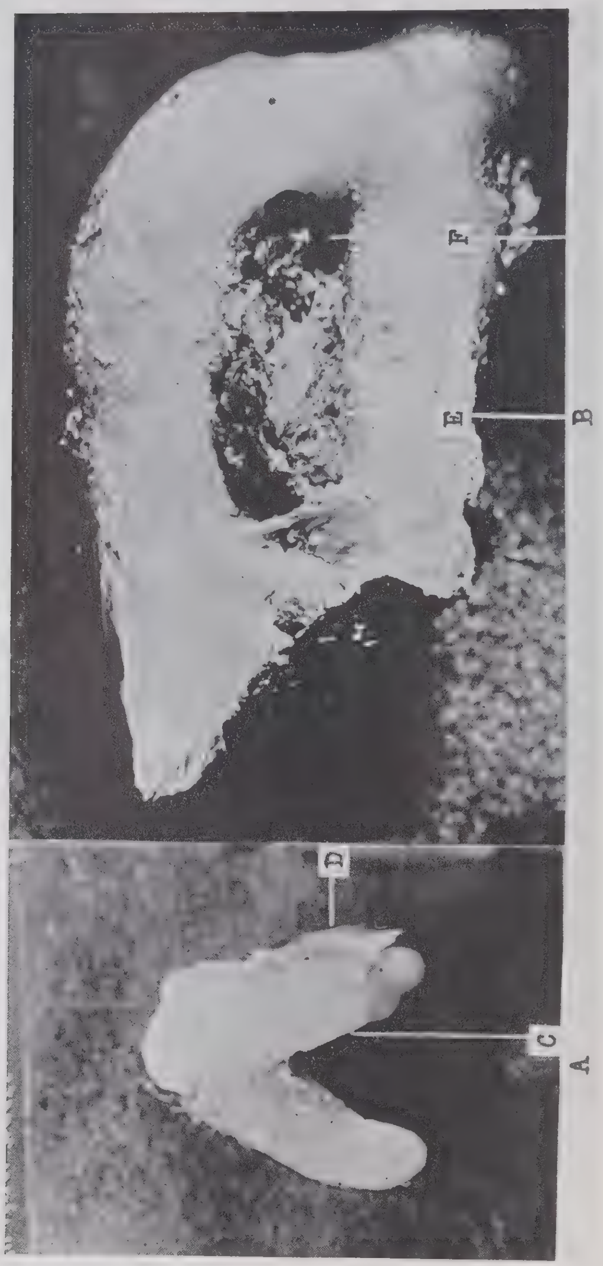


FIGURE 31. A AND B SHOW TWO VIEWS OF AN EXTRACTED MOLAR ROOT OF THE CASE SHOWN IN FIGURE 30, WITH MARKED EXCEMENTOSIS FUSING THE MESIAL AND BUCCAL ROOTS, AND AT D, THE FIRMLY ATTACHED PIECE OF ALVEOLAR BONE.

lar bone, and the same organism was found. C of Figure 29 shows this alveolar bone two years later, at which time the dense bone was becoming less dense. Incidentally, the patient improved after the extraction of these and other similar teeth so that she was able to get about on crutches, whereas formerly she had to be carried. Note that, in this case even the large quantity of infection in a half filled root canal of long standing, produced only a radiolucency without the development of granuloma. A lesser quantity of infection produced no radiolucency but a radiopacity. We are, in this patient, apparently dealing with forces which resemble in their effect those expressed in Figure 25, A-2 and B-3, and quite unlike those in Figure 25, A-1, B-1, and A-3.

A careful study of the various types of local reaction found resulting from dental infections was made as a part of this research by comparing different teeth in the same individual. This was done with a large number of individuals. Figure 30 is a typical illustration. Here it will be noted that the roentgenographic evidence of the condition would indicate a similar type of condition in the bone surrounding the roots of the many involved teeth. None had extensive absorption, notwithstanding the fact that we have the quantity of irritant that would be available from a putrescent pulp, as seen in the upper left first biscuspid and in the unfilled roots of the mesial root of the upper left first molar, all upper incisors, the mesial root of the lower right second molar, and the upper right first and second molars. The condition in this mouth, as revealed at the time of operation, showed that there was a very unusually dense bone about the roots of all the infected teeth, as also a marked excementosis of the roots of the upper left first molar which is shown in photograph in Figure 31. It will be noted that the mesiobuccal and distobuccal roots are fused together so completely as to be a continuous mass. When this root was extracted, the alveolar bone was so adherent that a piece of it came away with these roots, shown in Figure 31-B.

In striking contrast to this last case, we find many patients with very extensive areas of absorption about similarly involved teeth. Such a one is shown in Figure 32. In this case it will be noted, the upper central with very little evidence of unfilled root space has a very extensive zone of absorption, as does also the upper left first biscuspid and lower right first biscuspid; and this is the more important because the former was a young person and this patient is fifty-six years of age. The matter of the compari-

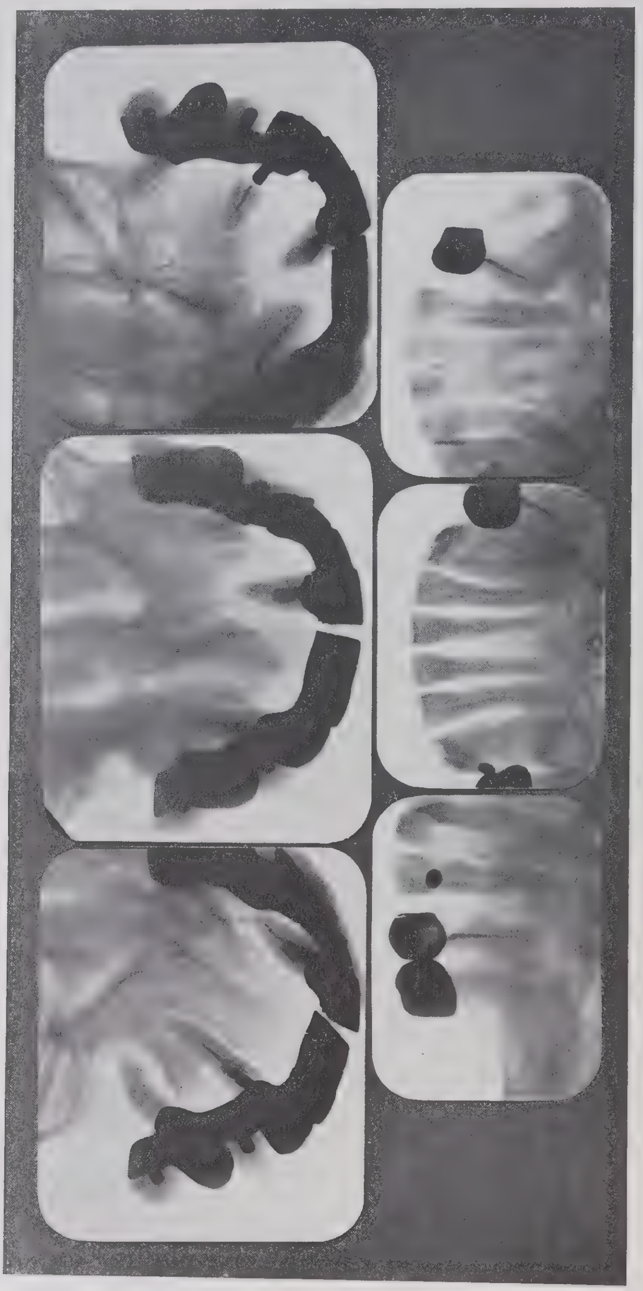


FIGURE 32 SHOWS EXTENSIVE ABSORPTION OF ALVEOLAR BONE ABOUT INVOLVED TEETH OF THIS INDIVIDUAL, IN CONTRAST WITH FIGURE 31.

son of the health of these two individuals is one which we will take up in subsequent chapters, for it has very direct and important bearing on the type of pathology.

A study was made of the different members of the family in a large series of families to ascertain whether the same general conditions tend to prevail; that is, whether a dental infection tends to produce the same type of tissue reaction about the teeth in the different members of a given family. Figure 33 shows a typical illustration of this study. In it we have the roentgenographic record of the reactions to dental infections in three sisters and a brother of the patient reported in Figure 31. It will be noted by comparison, for example, of the two roentgenograms shown in each A, B, C, and D, that there is a very marked similarity in the type of tissue change, as was also demonstrated at the time of surgical removal of these teeth in the clinical condition found. Note particularly the mesial root of the lower molar in A and part of the distal root of the same, give the same evidence of incomplete root filling, which condition also exists in the upper right second molar. B shows a similar condition of a lower and an upper molar; C does of a lower molar; and D of an upper molar and incisors. If quantity had been the all-determining factor, as expressed by the capacity of the space left in the unfilled root, these might all be expected to have large apical areas of rarefaction. In all the teeth of these various members of this family there was found not only the similar condensing osteitis but a very great tardiness in the healing process. The sockets tended to become infected and painful, requiring relatively long periods for the filling in of the alveolus. It should be noted that in addition to the similarity of these members of this family from the standpoint of the local structural reaction to dental infections, there was also a marked similarity in systemic involvements, all of which were breaking at from twenty to thirty years of age. This we have discussed in further detail in Chapter 59.

Similarly, in Figure 34, we have the roentgenograms of the teeth of the brother and sister of another family showing an entirely different type of reaction to dental infection. In this case there are areas of very extensive rarefaction about all involved teeth. At the time of surgical removal of these teeth it was found that, whereas in the last case they were all exceedingly difficult to extract and all surrounded by very dense bone, in this family they not only have roentgenographic evidence of exten-

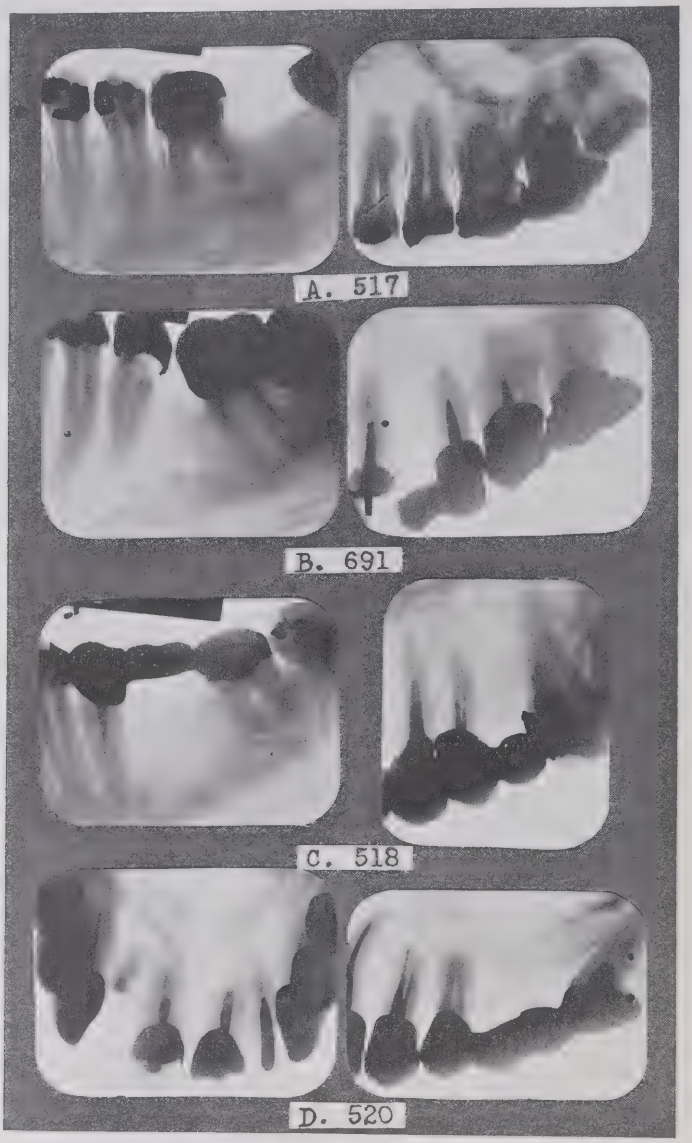
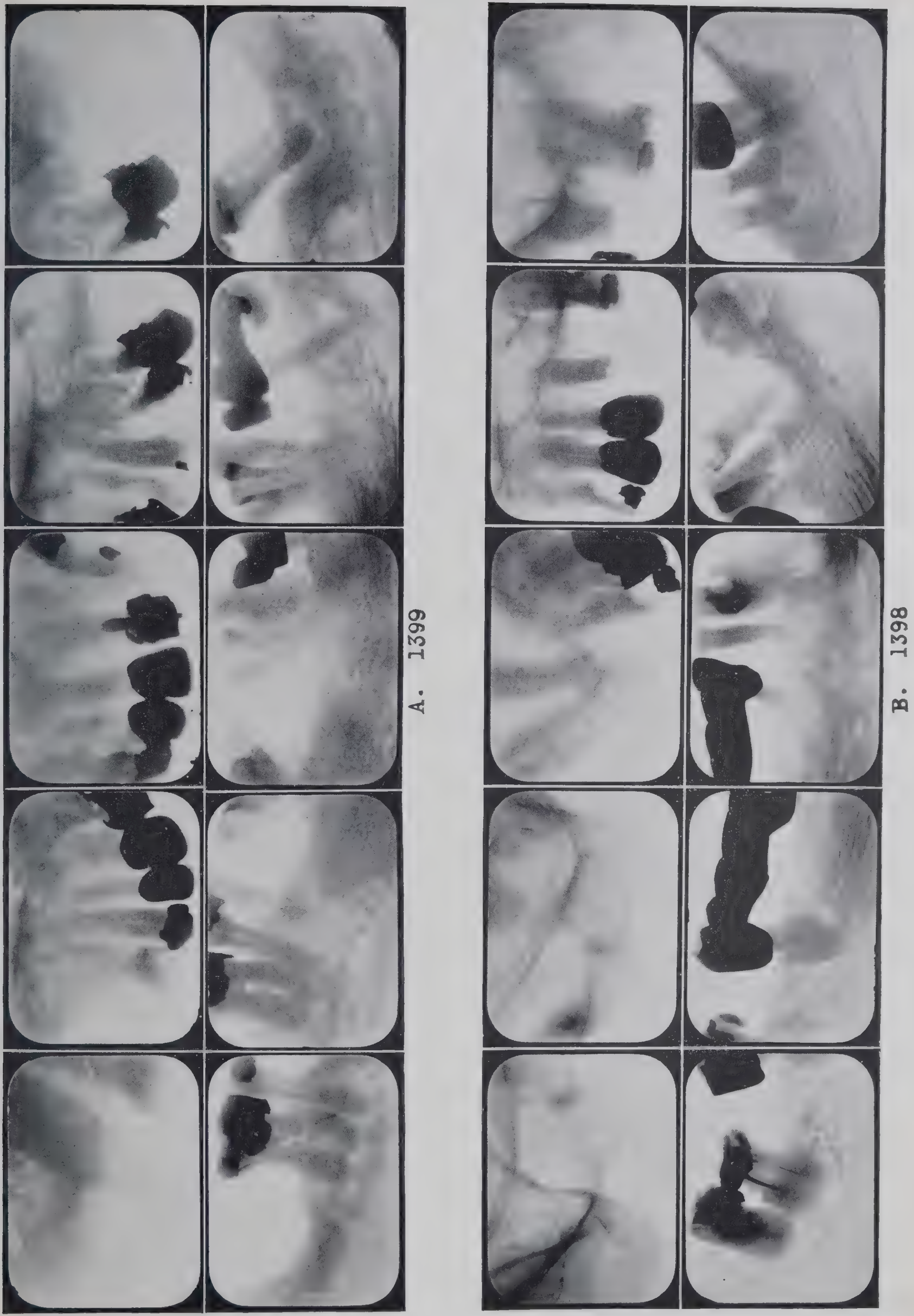


Figure 33. A comparison of the type of reaction in different members of the same family. Note the absence of apical reaction.

sive areas of absorption in all members of the family where dental infections exist, but at the time of surgical removal it was also found that there was a marked similarity in the structural conditions. The teeth were easily extracted; the bone was not dense about them; and the sockets healed with great rapidity and without discomfort or secondary infection. Nature in these instances did not require any assistance.

A study was then made to see in what different groups individuals could be placed, with regard to the type of reaction de-



A. 1399

B. 1398

FIGURE 34. A COMPARISON OF THE TYPE OF REACTION IN DIFFERENT MEMBERS OF THE SAME FAMILY. NOTE THE PRESENCE OF EXTENSIVE APICAL REACTION.

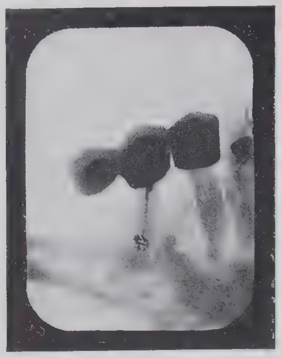


FIGURE 35. DIFFERENT TYPES OF REACTION ABOUT ADJOINING TEETH.

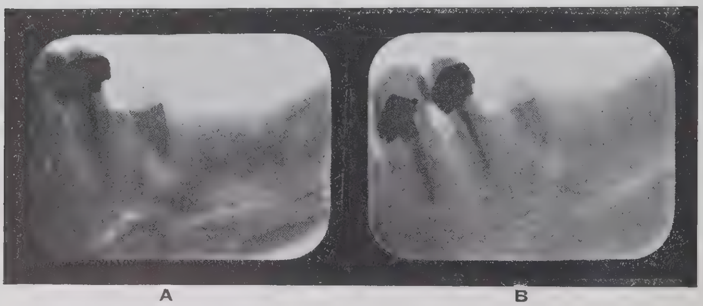


FIGURE 36. AN APPARENT IMPROVEMENT IN DENTAL CONDITION FOLLOWING BREAK IN HEALTH.

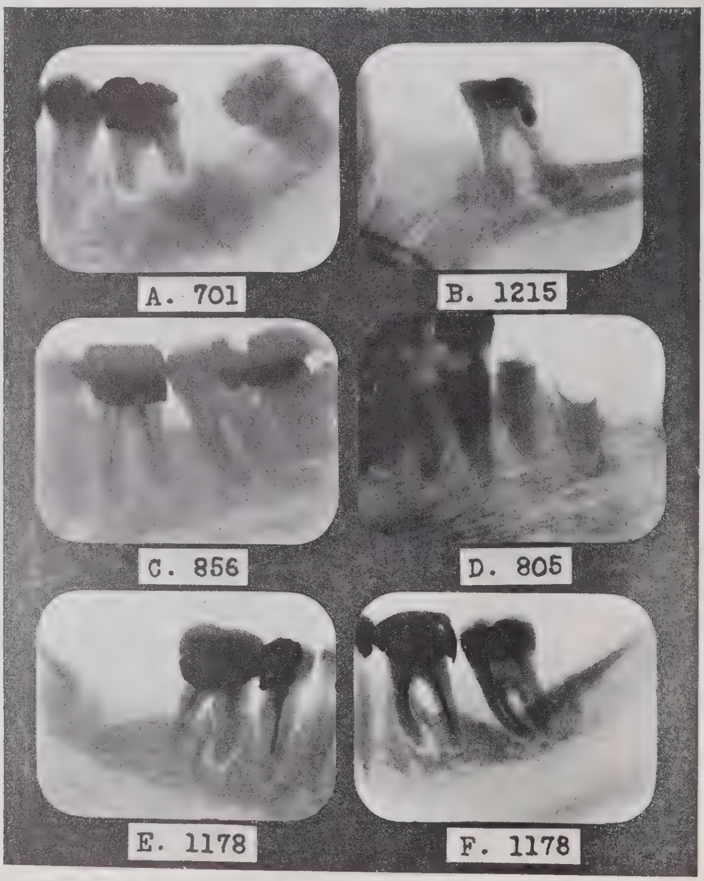


FIGURE 37. ROENTGENOGRAPHIC APPEARANCE OF CONDENSING OSTEITIS ABOUT INFECTED TEETH.

veloping in tissue, as a result of various types of dental infections, and it was found that in addition to the two types illustrated above, there was frequently found a type which was similar in many respects to that in Figure 34, except that the area of rarefaction seemed bounded by a zone of more dense bone, as it were, a zone of condensing osteitis around one of rarefying osteitis. This type is illustrated in Figure 37. It was found that the various patients having this type of condition were comparable in that the teeth were frequently difficult to extract, often had a history of a fistula having existed previously, and closing sockets did not heal as readily as the type in Figure 34. In many respects individuals of this class presented sockets that were similar to those in Figure 33 in the condition found clinically and the difficulties attending the healing process, while the conditions roentgenographically resembled in a general way in that there were frequently large areas of absorption, the type of reaction found in the group as shown in Figure 34.

While extensive rarefaction as a result of infection, and condensation or absence of rarefaction, may be typical expressions of different types of systemic reaction, therefore appearing in different individuals with different physical characteristics, it is possible to find both these conditions in the same individual, as shown in Figure 35 which shows a very marked area of alveolar absorption around the root of the first biscuspid with no absorption around the second biscuspid, which latter has an excementosis. This will appear to some like a contradiction. It probably is due to the following conditions: It will be noted that the first biscuspid with its large area of absorption has a zone of condensed bone surrounding that zone of rarefaction; also that it has evidence of an absorption process on the root; and this tooth had all the infection of the unfilled pulp canal in addition to the infected dentin as a source of irritation. The second bicuspid has a root filling and probably has very much less total infection and capacity for toxic material than the first bicuspid. It is also probable that in addition to this great difference in quantity, the condensing osteitis of the first bicuspid has formed during a period succeeding the period during which the absorption developed; and it will be shown later that the condition of excementosis about the second bicuspid has probably taken place during the period in which the condensing osteitis surrounding the rarefying osteitis

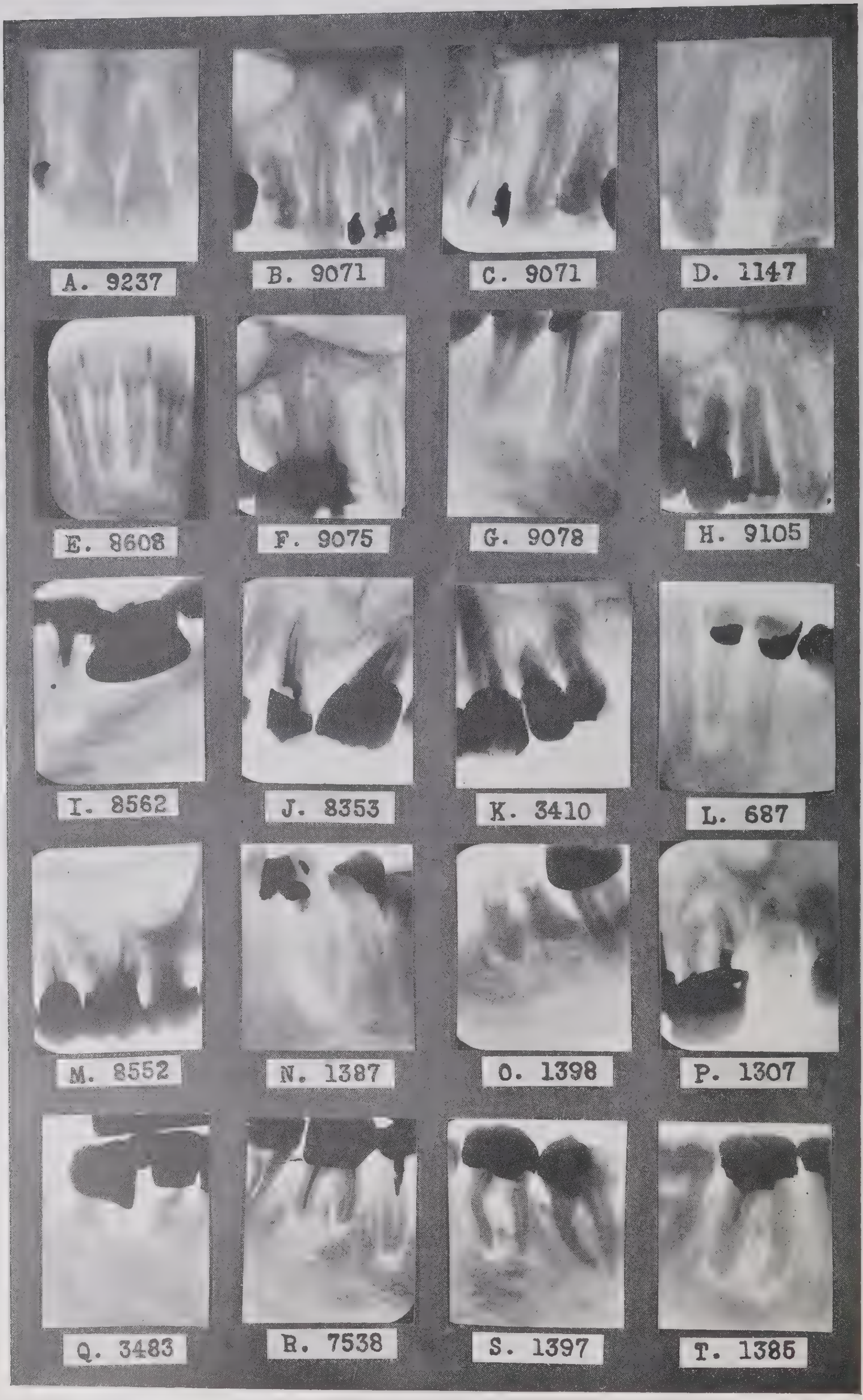


FIGURE 38. A GROUP SHOWING EXTENSIVE RAREFYING OSTEITIS ABOUT INFECTED TEETH.

occurred about the first bicuspid. Just as in geology the recorded depositions may represent entirely different conditions because they occur in different periods, similarly, recorded bone changes may chronicle entirely different types of reaction because they belong to different periods; in other words, one of the important elements involved is the environment, together with the fact that a small quantity of irritation may be sufficient to produce just enough stimulation to make a deposition; whereas, a much larger quantity goes beyond the point of stimulation to irritation and produces rarefaction.

If, as we have suggested, individuals may change their capacity for reaction to a given dental infection, we should find evidence of this about teeth which have not been subjected to surgical interference or medication. Such a condition is shown in Figure 36 in which in A we have the extent of the zone of rarefaction about an infected bicuspid root and which six months later, as shown in B, has a smaller area. It is not probable that the infection has become less serious either in virulence or quantity. There is an important relationship, however, to the patient's health which will come out in the next chapter.

We have, accordingly, studied carefully a very large number of roentgenograms covering all of those in a busy clinical practice for many years, and have found evidence in the roentgenograms to suggest their classification into three main groups on the basis of the type of structural change produced in the supporting structures about infected teeth. We have, accordingly, made up a page of each of these three groups: namely, those in which there is evidence in the roentgenogram of a vigorous reaction about the tooth, expressing itself with extensive absorption of alveolar bone and in some instances with absorption of the roots themselves. We have placed the centrals and laterals at the top, bicuspids next, and molars at the bottom. Figure 38 shows the group with this splendid reaction.

In the next group (Figure 39) we have presented those in which there is evidence of a change in the type of reaction in which there has been originally a very abundant absorption, but about the periphery of which absorption area there is evidence of a condensed layer in contrast with the preceding group in which in many or most instances the zone diffuses off into cancellous bone. Whereas the medullary spaces are frequently enlarged and have direct connection with the absorption chamber, in this group there

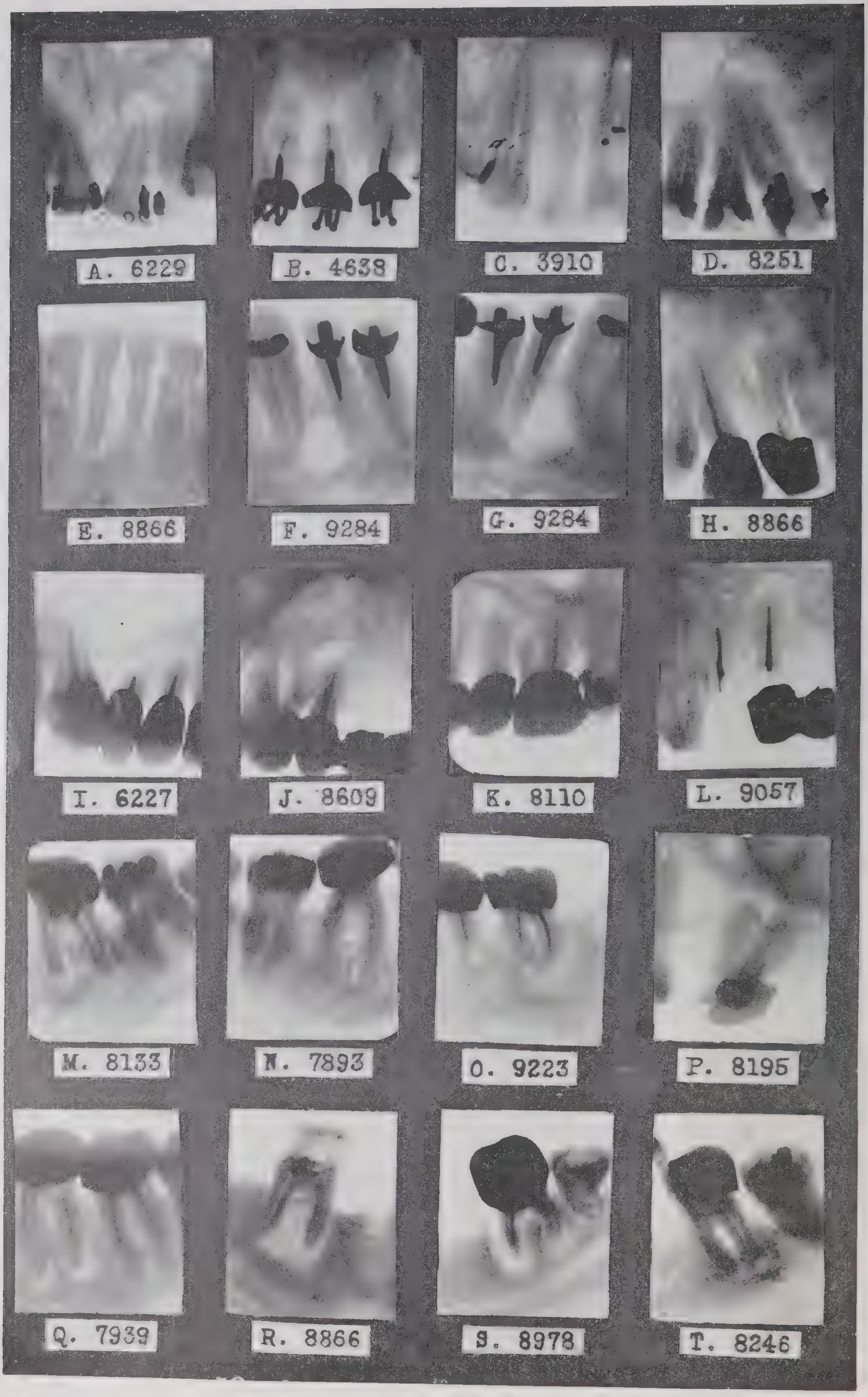


FIGURE 39. A GROUP SHOWING A ZONE OF CONDENSING OSTEITIS SURROUNDING A ZONE OF RAREFYING OSTEITIS ABOUT INFECTED TEETH.

is a reduction in the medullary spaces with an enlargement of the trabeculae adjoining the absorption chamber, which latter is frequently surrounded by a dense continuous bony shell, often polished like the inside of an egg shell, with occasional or very few connections with the medullary spaces. There is evidence of distinct change in the progress of this reaction; whereas there was one time an active absorption with enlargement of the chamber, there is now a deposition at the periphery of the granulomatous tissue with the obliteration of the medullary spaces.

A third group is shown in Figure 40, in which there has never been an extensive zone of absorption about the root apices and in many instances there seems to have been much obliteration of the cancellous structure of the bone. The medullary spaces are small or lost by the fusing of the trabeculae. In this group there is no evidence of there ever having been a fistula. The teeth were seldom, if ever, tender. There is very little reaction about the tooth and what there is, is largely a deposition process about a very small zone of rarefaction.

Clinically, there are many characteristics in common in the members of these groups but in contrast with those of the other groups. For example, in the teeth of the first group there is generally a fistula with recurring exacerbations of tenderness or painfulness. This is continued to the present. The sockets left after the extraction of the teeth of the first group tend to heal readily without treatment or tendency to local infection. The members of the second group often show the evidence of an old scar of a fistula but none, of late. Formerly the tooth got tender but not so, recently. These teeth tend more to infection of the sockets following extractions than those in Group 1 and require more postoperative care after exodontia. Those in Group 3 never had a fistula; seldom, if ever, became tender; the sockets tend very readily to infection after exodontia, often very painful requiring careful postoperative care, for both this group and the one preceding tend readily to develop what is frequently referred to as dry socket following extraction, which the former group in Figure 38 never does. Another characteristic of the groups will be that the teeth in Group 1, Figure 38, tend to be extracted easily, those in Group 2, Figure 39, quite difficult, and those in Group 3, Figure 40, often exceedingly difficult. With regard to infiltrative anesthesia, those in Group 1 are very readily anesthetized; those in Group 2 less so; and those in Group 3 tend to be very difficult.

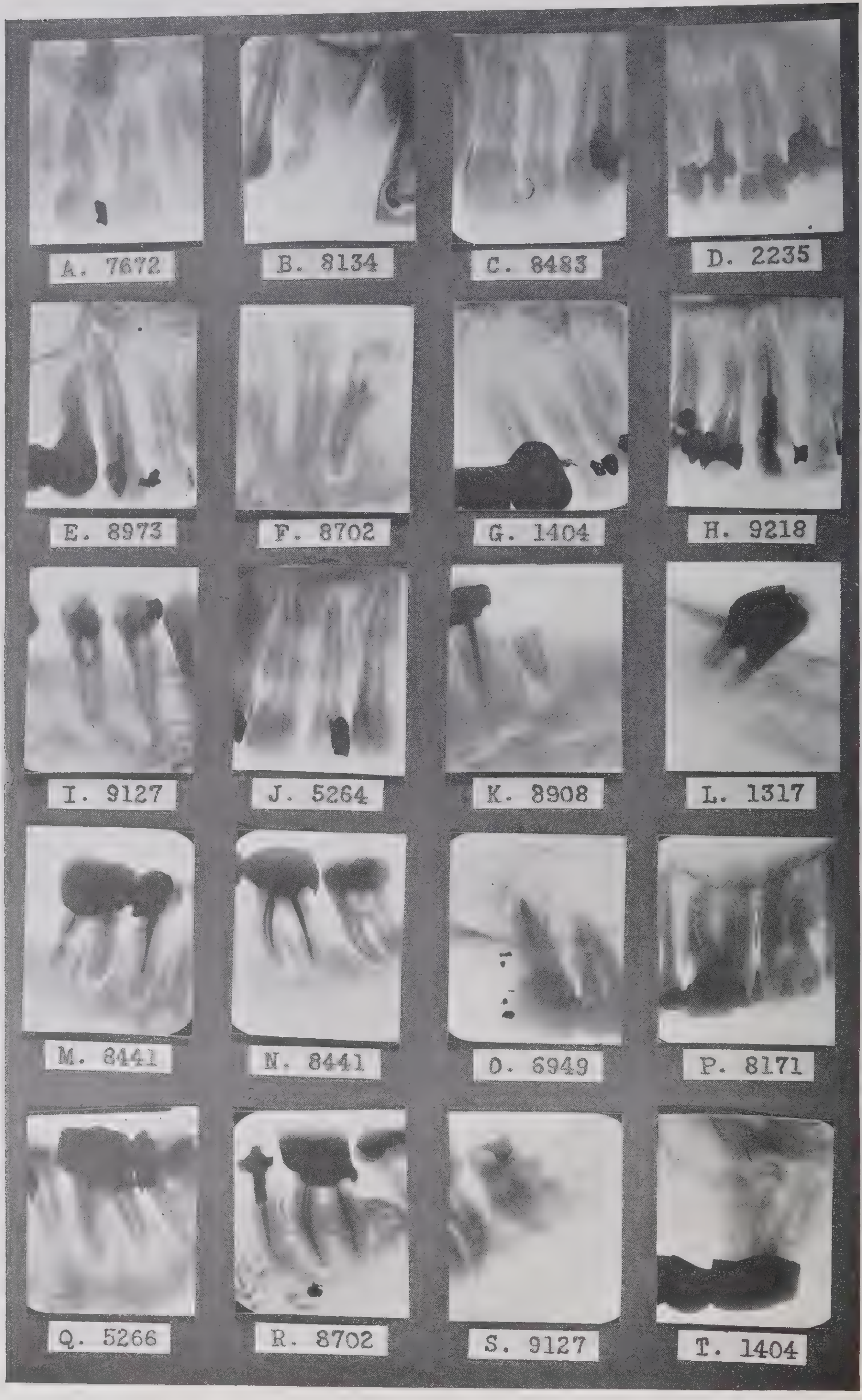


FIGURE 40. A GROUP SHOWING LIMITED REACTION, WITH OR WITHOUT CONDENSING OSTEITIS, ABOUT INFECTED TEETH.

SUMMARY AND CONCLUSIONS.

1. An analysis of these data reveals that the first premise—namely, *that infection will express itself in bone as absorption*—is not a constant finding, assuming that the quantity of infection that would be represented by an infected pulp of a single rooted tooth represents approximately the same quantity for a given tooth in various individuals. The extent of absorption is not the same in all these individuals, for there may be very extensive absorption in one case and in the very next case very little absorption or a previous deposition of bone, or both. And this difference is not explainable on the basis of quantity; for, indeed, it will often be found that whereas in some cases the local effect of the quantity of infection represented in large pulps which are putrescent, therefore large quantities of infection, may be exceedingly small; and in other cases with even very small pulps or nearly filled pulp chambers, or even completely root-filled canals, there will be enough irritation to produce very large areas of absorption.

2. With regard to the matter of grouping of individuals, it is very evident that members of the same family tend to have the same type of reaction about their teeth, immediately suggesting an evidence of grouping.

3. Frequently in the study of individuals we find cases with quite extensive absorption but which areas are surrounded with zones of apparently dense bone. These individuals seem clearly to have had a change come into their lives. They have at one time been in the first group and have finally come to be in the second group. As a class these individuals are so characteristic that they can readily be put into a group by themselves on the basis of the local structural change about their teeth; for the inoculation of experimental animals with cultures taken from dental sources has revealed variations in conditions which vary through a wide range, from very marked absorption of bone to very definite deposition within the bone.

We can therefore briefly summarize as follows:

(a) Dental infection in bone may express itself as absorption, even extensive absorption, or may be attended by very little or no absorption, or may even produce a marked increase in the density of the bone. (b) A given dental infection will not express itself in the local tissues of the mouth approximately the same in all people. People tend to divide into groups with regard to this matter of local reaction, which groups are very dissimilar.

CHAPTER IV.

SYSTEMIC STRUCTURAL AND FUNCTIONAL CHANGES PRODUCED BY DENTAL INFECTIONS.

PROBLEM: Are all human beings similar or sufficiently so that they may be considered comparable in their reactions to dental infections?

INTRODUCTION.

If, as seems indicated from the preceding researches, the presence or absence of systemic involvements and their nature is not dependent primarily upon biological characteristics of the organisms involved, and if the local structural changes about the teeth are not the same in different individuals for a given or similar type of infection, there is strong evidence that other factors must be responsible for the presence or absence of local and systemic effects from dental infections. Historically, about all that has appeared in the literature has been a reference to a rheumatic diathesis influenced by racial, climatic, geographic, industrial, and environmental conditions.

EXPERIMENTAL AND DISCUSSION.

A fundamental law of biology, physics, and chemistry, is that similar causes produce similar effects; and since this is a biological problem, it has been very natural to suppose that even though the factor involved in the invading organism is variable, the factor involved in the host is a common and universal one. In fact, a department of applied medicine is based on this assumption: namely, clinical pathology or diagnosis. Not that all people exposed to typhoid develop a typical case of typhoid fever, but that those who do become a prey to this infection develop similar symptoms; and upon this symptomatology the disease is identified. This presupposes (1) that the invading typhoid organisms will, in general, have the same powers of attack varying within certain limits in severity, selecting the same tissues, and (2) that the reactions in the patient will be clinically similar. This being true of a great majority of pathogenic organisms has made it possible for a very general and quite effective classification of infectious diseases to be made, whether the infection entered the system by the respiratory tract, the digestive tract, or by implantation within the tissues. The invasion of the organisms has resulted in local and general tissue reactions which have been termed symptoms, and on this the whole department of clinical medicine or clinical diagnosis has been based. The near universality of this rule of symptomatology has made it very natural and logical that the same general fundamental principles would be understood to apply to both the aggressive qualities of the organisms in dental infections and the reactions of the host to such an infection if it existed.

Applying this general law of clinical medicine, we have concluded that people who are well, or are not ill, are not infected; and, similarly, teeth that are well, or at least not ill, are not infected; and teeth that have been ill and have become apparently well have ceased to be infected. The answer to the questions "What constitutes a sick or afflicted tooth?" and "What are the symptoms of an infected tooth?" has been determined by the same law of symptomatology. Since, with practically all infections the severity of the symptom is an expression of the severity of the involvement, therefore we have argued that teeth with serious inflammatory processes, whether in the pulp which is so capable of expressing abnormal states or in the peridental membrane, a tissue nearly as responsive, are or are not seriously infected in proportion to the pain and evidences of inflammation involved. This has implied that the attacking power of the invading organisms, the reacting power of the host, and the resultant of the reaction—namely, the clinical symptoms—will be comparable in various individuals as well as in various teeth of the same individual.

To determine this we have made a very careful analysis of fourteen hundred cases in order that we might ascertain the correctness of this presumption. We have undertaken to establish, so far as was feasible, the following factors: The characteristics of the host, including susceptibility to caries and susceptibility to gingival infections or periodontoclasia; the characteristics of the local histopathology; the tendency to systemic involvements and their kind; whether there is a definite susceptibility to the type of organism usually found in dental infections; whether that factor has developed recently, or whether it has been the characteristic throughout life; whether it is an inherited characteristic, whether its dominance is marked, and whether inherited from both sides of the ancestry; and the effects of overloads and the nature of those most involved.

We have found it very difficult to establish what might be considered a normal individual; and, in any group, to know how divergent they of that group are from the normal; or, of the individuals studied, what percentage any group might form of the total of society. We have undertaken to establish what might be considered normal individuals by selecting from those examined those most free from systemic involvements. We have accordingly found a very constant grouping of individuals which we shall later analyze in detail. The Chart in Figure No. 41 shows the general result of this study.

INTERPRETATION OF RESULTS OF SUSCEPTIBILITY EXPERIMENTATION

Many very interesting and unexpected units of information have been revealed, which seem to establish very definitely that human beings are not similar in the sense that the same rules can be applied to all and various individuals for the interpretation of the immediate symptoms or of their significance. In general we find that all individuals divide naturally into two main groups so far as the presence or the probable presence of systemic reactions to dental infections is concerned. We have chosen to call these groups *non-susceptibles* and *susceptibles*. The latter group, the *susceptibles*, naturally subdivides into two. The first is a group whose susceptibility is an *acquired* factor. It is made up of people who belong in the non-susceptible group, but who, because of various forms of overload which will be discussed later, have come into the group we have termed *acquired susceptibles*. There are many things which distinguish this sub-group from the balance of the general groups we have called susceptibles. The second division of the susceptibles has characteristics which are so outstanding that they make themselves readily recognized. They have never been in the first group, or non-susceptibles, and while they may not have broken during long periods of their life, they have tended to break with the presence in the system of the type of infection requisite for making manifest that inherited susceptibility. This type of infection, as will be seen, is found in practically all dental lesions. There seems to be truly an inherited quality which, as is disclosed, shows very definitely evidences of

RHEUMATIC GROUP LESIONS OF INDIVIDUALS AND THEIR RELATIVES

Susceptibility Studies by Alphabetical Groups

							Number of Lesions of Individuals							Number of Relatives Affected						Number of Lesions in Individuals and their Families											Number of Lesions Severe and Severe and Mild in the Three Susceptibility Groups														
																																Inherited					Acquired					Absent			
Alphabetical Group	Total Number	Average Age	Male Number	Average Age	Female Number	Average Age	Tonsils	Rheumatism	Heart	Neck	Nerves	Internal Organs	Special Tissues	Brothers	Sisters	Father	Father's Relatives	Mother	Mother's Relatives	Tonsils	Rheumatism	Heart	Neck	Nerves	Internal Organs	Special Tissues	Total Severe	Per cent Severe	Total Severe and Mild	Per cent Severe and Mild	No. Pat's in Group	Severe	Average Severe	Severe and Mild	Average Severe and Mild	No. Pat's in Group	Severe	Average Severe	Severe and Mild	Average Severe and Mild	No. Pat's in Group	Severe	Average Severe	Severe and Mild	Average Severe and Mild
A	18	41.6	5	44.6	13	40.4	13	13	5	12	16	12	14	13	13	15	9	16	11	28	65	35	23	131	50	37	278	15.4	369	20.5	11	220	20.0	286	26.0	6	53	8.8	77	12.8	1	5	5.0	6	6.0
B	28	42.0	6	37.1	22	43.3	16	17	10	17	25	18	23	12	20	24	14	21	14	37	69	39	29	164	96	57	310	11.1	491	17.5	14	219	15.6	301	21.5	8	60	7.5	113	14.1	6	31	5.2	77	12.8
C	41	42.0	15	41.7	26	42.2	22	22	12	21	29	23	24	19	23	30	16	25	21	47	98	48	35	163	139	66	417	10.2	596	14.5	20	307	15.3	431	21.5	10	62	6.2	85	8.5	11	48	4.4	80	7.3
D	3	36.0	0		3	36.0	1	3	2	3	3	2	3	2	2	2	1	3	3	8	20	14	9	29	10	24	53	17.6	114	38.0	3	53	17.7	114	38.0										
B2	46	43.9	14	47.6	32	42.3	16	29	12	28	39	33	26	23	27	34	17	32	22	29	93	50	38	239	157	58	495	10.8	664	14.4	25	365	14.6	473	18.9	15	113	7.5	160	10.7	6	17	2.8	31	5.2
D	27	43.0	8	47.6	19	41.0	13	18	6	18	22	13	19	16	10	22	9	21	9	27	76	34	33	156	71	70	302	11.2	467	17.3	13	201	15.5	326	25.1	8	50	6.2	77	9.6	6	51	8.5	64	10.7
E	11	42.6	3	38.7	8	44.1	8	7	2	6	11	10	7	7	8	7	4	5	7	9	24	8	9	42	38	16	106	9.6	146	13.3	5	67	13.4	86	17.2	4	30	7.5	45	11.2	2	9	4.5	15	7.5
F	11	43.0	7	39.6	4	49.0	8	5	4	7	9	8	9	8	5	9	5	8	6	18	30	18	12	33	42	27	97	8.8	180	16.4	4	48	12.0	83	20.7	3	26	8.7	50	16.7	4	23	5.7	47	11.7
FG	59	43.4	18	48.3	41	41.2	28	33	17	38	48	31	43	25	22	35	16	47	28	56	108	73	51	281	137	111	543	9.2	817	13.8	32	388	12.1	583	18.2	19	130	6.8	198	10.4	8	25	3.1	36	4.5
H	44	44.0	6	51.5	38	42.8	19	32	8	28	33	26	26	20	21	33	14	37	24	37	110	49	45	208	148	69	486	11.0	666	15.1	30	401	13.4	533	17.8	7	57	8.1	81	11.6	7	28	4.0	52	7.4
I	4	43.2	0		4	43.2	3	3	2	2	3	3	3	3	2	3	1	3	1	3	19	7	3	46	21	13	85	21.2	112	28.0	3	84	28.0	111	37.0						1	1	1.0	1	1.0
J	17	37.4	4	39.0	13	36.8	7	8	4	12	14	8	14	9	8	12	4	11	5	15	28	16	14	62	37	22	128	7.5	194	11.4	8	91	11.4	125	15.6	6	31	5.2	51	8.5	3	6	2.0	18	6.0
K	33	37.2	10	36.2	23	37.7	21	20	3	18	29	20	22	19	21	27	14	27	16	58	120	42	57	294	158	115	616	18.7	844	25.6	17	505	29.7	663	39.0	10	89	8.9	142	14.2	6	22	3.7	39	6.5
L	29	38.0	8	39.6	21	37.4	16	18	9	21	26	20	22	15	19	21	15	23	19	31	72	36	38	194	86	64	360	12.4	521	17.9	21	311	14.8	441	21.0	4	27	6.7	48	12.0	4	22	5.5	32	8.0
M1	12	44.2	3	37.7	9	46.3	4	8	2	8	11	10	11	7	7	11	2	10	7	9	32	9	14	73	41	20	155	12.9	198	16.5	8	120	15.0	151	18.9	2	26	13.0	31	15.5	2	9	4.5	16	8.0
M2	56	37.4	12	36.1	44	37.7	34	36	13	29	45	31	41	27	29	41	22	48	33	71	152	79	46	320	179	114	657	11.7	961	17.2	39	568	14.6	804	20.6	14	77	5.5	140	10.0	3	12	4.0	17	5.7
P	35	42.2	11	49.0	24	39.1	13	23	6	18	24	22	19	12	12	22	12	27	19	35	71	47	29	147	97	65	300	8.6	491	14.0	17	215	12.6	358	21.1	11	51	4.6	85	7.7	7	34	4.9	48	6.9
NO	18	35.3	5	39.4	13	33.7	9	13	10	11	14	8	12	9	9	15	8	14	10	29	71	43	34	128	78	54	317	17.6	437	24.3	14	301	21.5	412	29.4	3	13	4.3	20	6.7	1	3	3.0	5	5.0
R	17	44.9	7	46.6	10	43.7	7	11	2	7	12	7	10	10	6	12	4	12	8	12	35	10	9	68	46	20	147	8.6	200	11.8	9	90	10.0	122	13.6	7	57	8.1	78	11.1	1	0	0.0	0	0.0
S1	36	43.2	13	47.4	23	40.9	23	23	6	21	30	24	21	14	14	26	18	26	15	32	72	47	31	160	121	39	370	10.3	502	13.9	24	300	12.5	404	16.8	4	31	7.7	47	11.7	8	39	4.9	51	6.4
S2	20	41.4	8	44.2	12	39.5	8	13	6	11	16	10	12	10	11	16	6	15	8	16	42	26	16	89	50	35	183	9.1	274	13.7	13	148	11.4	207	15.9	5	30	6.0	54	10.8	2	5	2.5	13	6.5
T	25	44.1	8	40.6	17	45.7	16	18	8	20	24	17	21	15	10	17	12	21	14	28	62	45	27	155	70	41	320	12.8	428	17.1	19	282	14.8	374	19.7	3	26	8.7	37	12.3	3	12	4.0	17	5.7
V	9	44.4	5	39.2	4	51.0	2	3	2	6	8	5	8	6	4	3	3	8	2	2	15	3	9	48	13	16	70	7.7	106	11.7	4	41	10.2	63	15.7	5	29	5.8	43	8.6					
W	55	39.7	15	40.5	40	39.4	35	35	15	34	43	29	38	30	29	41	24	46	29	65	131	96	51	289	164	102	628	11.4	898	16.3	34	524	15.4	730	21.5	12	80	6.7	117	9.7	9	24	2.7	51	5.6
YZ	9	34.5	2	31.0	7	35.6	7	5	5	6	7	5	6	6	3	5	4	8	3	12	21	13	7	41	24	20	91	10.1	138	15.3	6	78	13.0	108	18.0	3	13	4.3	30	10.0					
S3	18	41.7	6	43.2	12	40.9	11	12	5	14	14	11	14	9	13	15	9	15	12	24	54	29	21	99	53	43	208	11.6	323	17.9	12	168	14.0	261	21.7	5	36	7.2	54	10.8	1	4	4.0	8	8.0
Totals	681	1070.3 41.2	199 29%	1006.4 41.9	482 71%	1070.9 41.2	360	428	176	416	555	406	468	346	348	498	263	529	346	738	1690	916	690	3659	2126	1318	7722	307.1 11.8	11137	453.4 17.4	405	6095	398.5	8550	570.4	174	1197	170.0	1863	265.2	102	430	89.9	724	152.4
							Average Number of Breaks per 100 Individuals in							Percentage of Relatives Affected						Average Number of Breaks per Family in											Average Number of Lesions Severe, and Severe and Mild, per Susceptibility Group														
																																Susceptibility Inherited					Susceptibility Acquired					Susceptibility Absent			
							53	63	26	61	81	60	70	51	51	73	39	78	51	1.08	2.48	1.35	1.01	5.37	3.12	1.94	11.34	11.34	16.35	16.35	59	15.05	15.3	21.11	21.9	26	6.88	7.1	10.71	11.0	15	4.22	4.1	7.098	6.9
							Tonsils	Rheumatism	Heart	Neck	Nerves	Internal Organs	Special Tissues	Brothers	Sisters	Father	Father's Relatives	Mother	Mother's Relatives	Tonsils	Rheumatism	Heart	Neck	Nerves	Internal Organs	Special Tissues	Average Severe		Average Severe and Mild			Average Severe		Average Severe and Mild			Average Severe		Average Severe and Mild			Average Severe		Average Severe and Mild	

(Note: This chart is a consolidation of 140,000 determinations some of which took minutes, and some hours of time.)

The summary at the right (bold face) is an analysis of the susceptibilities of the patients and their families to the rheumatic group lesions

SUMMARY

Susceptibility *Inherited*
Average Severe 15.05
Average Severe & Mild 21.11

Susceptibility *Acquired*
Average Severe 6.88
Average Severe & Mild 10.71

Susceptibility *Absent*
Average Severe 4.22
Average Severe & Mild 7.089

FIGURE 41.

the laws of mendelism. Accordingly, we have divided all individuals into three main groups: the first, those with non-susceptibility; the second, those with an acquired susceptibility; and the third, those with an inherited susceptibility. An illustration familiar to everyone from earliest recollection will be the common phrase "Heart disease runs in this or that family."

A detailed description of what is presented in the chart in Figure 41 is as follows: The letters of the alphabet, called "Alphabetical Group," represent the first letter of the patient's name in order that a comparison may be made of as many different groups as there are letters of the alphabet for the purpose of showing the constancy of percentages, etc. The succeeding columns are "Total Number per Alphabetical Group, Average Age, Number of Males, Their Average Age, Number of Females, Their Average Age." The next section of the chart is entitled "Number of Rheumatic Group Lesions (past and present) of the Individual Being Studied" under which we have Tonsils, Rheumatism, Heart, Neck, Nerves, Internal Organs, and Special Tissues. The next division entitled "Number of Relatives Affected" indicates the number of instances in the group where Brothers, Sisters, Father, Father's Relatives, Mother, Mother's Relatives were affected with rheumatic group lesions. The next column is a combination to show the number of Severe, and Severe and Mild instances of rheumatic group lesions of the patient and family. These include the subdivisions of Tonsils, Rheumatism, Heart, Neck, Nerves, Internal Organs, Special Tissues, Total Severe Lesions (by which we mean those severe enough to incapacitate them or put them to bed or cause death), Percentage Severe, Total Severe and Mild Lesions, and Percentage of Severe and Mild.

The balance of the chart, which is divided into three main groups, consists of a study of the number of lesions severe, and severe and mild, in the three susceptibility groups, *inherited*, *acquired*, and *absent*. In all of these three groups we have in the first column the number of patients in the group, followed by the severe lesions, the average severe lesions, the severe and mild lesions, the average severe and mild lesions. It will be noted that if the figures showing percentage in any of the three groups, as, for example, Average Severe or Average Severe and Mild, are read downward, they show a marked similarity in those collections of patients which would be represented by the first letters of their names.

The figures at the bottom of the chart show the average number or percentages as per the various groupings as expressed. The heavy black leaded summary at the bottom gives the condensed summary of this very extensive study. The data here revealed constitute what I believe to be one of the most fundamental and far-reaching, but generally overlooked, forces operating to determine the nature of the systemic expressions of dental infections.

In a group of non-susceptibles consisting of 102 persons, which included all of those who did not have rheumatic group expressions (degenerative diseases) and never had had, either from dental or other origin, which were found in 681 cases selected from about 1400 because the records of their cases were considered sufficiently detailed and exact for scientific and comparable study, we find that this factor of immunity of the persons of this group consisting of 102 individuals, pertains in general also to all the other known members of those family circles; by which, we mean the immediate individuals in three generations: namely, the brothers and sisters of the individual, his or her father and mother and their brothers and sisters, and the grandparents of the individual.

We have termed the group of lesions produced by streptococcal infection the *Rheumatic Group* lesions, and have selected for our classification only such as were severe enough seriously to distress or incapacitate the patient. When we compare first the individuals in these three groups of absent susceptibility, acquired susceptibility, and inherited susceptibility, we find a very remarkable difference in their tendency to affections of the rheumatic group lesions. But even more striking and significant it is to find that this same quality tends to run as a constant law through the other members of their families; for, whereas the average number of severe rheumatic group lesions in the individual and the entire family as outlined is in the absent group only 4.2, in the acquired group it only increases to 6.8, but in the inherited group jumps to the remarkable figure of 15.05. And even more striking is the comparison of the average incidence of the severe and mild rheumatic group lesions which in the absent group is 7, acquired susceptibility group 10.7, and in the inherited susceptibility group jumps to 21.1.

I repeat this is one of the most important new truths that has been presented on this whole problem of the relationship existing between focal infections and the deficiency and degenerative diseases. Its significance cannot possibly be appreciated by simply reading it; for when the diagnostician thoroughly visualizes this great new truth, he will find himself playing the game of diagnosis with marked cards. He can pretty nearly make out either the patient's chart from the family record or *vice versa*. Immediately it will be realized that if the factor of danger is entirely different in these different groups, the factor of responsibility increases with that danger, and also that the individuals in the latter group must have an entirely different set of standards as to what shall be condemned or retained, from those with the much larger factor of safety. This will be developed in detail in the succeeding chapters.

The reader should have in mind in studying these results that the patients coming to a dental clinic such as this, include a much larger percentage of individuals with definite involvements than those found in an ordinary practice, since we have been specializing in dental diagnosis, dental pathology, and dental research. The percentages cannot, therefore, be considered as directly applicable to either the groups that would be made up in some other practice, or with the average people on the street.

We desire at this point to explain in a general way the method of making these examinations, and the detailed analysis of the method of diagnosis will be found in Chapter 59. On the presumption that there is more or less danger of exposure to rheumatic group lesions for every individual, differences in the prevalence of a break might furnish information that would help to point to the characteristics of individuals which have or have not a high defense, and by studying large groups we would be more likely to select those fundamental qualities which are characteristic and causative, or at least contributing factors. We have assumed that many individuals know whether or not they have had acute pain in their joints which has put them to bed, or have had a sense of being short of breath and exhausted from going upstairs, which their physician has told them was due to a condition of their heart, etc.; and that they could be depended upon in a general way to have information that would be of value for comparison, if not always exact. I can anticipate with relative certainty, based on past experience, that it will be argued that an individual will not know whether the parents and their brothers and sisters died of heart trouble or Bright's disease, or had rheu-

COMPARISONS OF SU

Susceptibility Class	Age	No. 100		Patients' Lesions in %												
		M	F	Tonsils	Rheumatism	Heart	Neck	Nerves	Internal Organs	Special Tissues	Brothers	Sisters	Fathers	Fathers' Relatives	Mothers	Mothers' Relatives
Averages of Total No.	41.3	29	71	53	63	**26**	61	81	60	70	51	51	73	39	78	51
Groups of 15																
Absent	40.7	53	47	27	13	**0**	13	13	7	7	0	0	27	7	33	20
Acquired	47.9	40	60	40	47	**20**	53	87	53	53	27	7	13	0	13	0
Inherited 1 side mild	43.4	33	67	53	93	**13**	60	80	47	47	33	47	60	40	67	60
Inherited 2 sides mild	40.9	20	80	60	87	**40**	73	80	67	73	60	73	80	47	93	73
Inherited 1 side strong	39.4	27	73	47	93	**27**	80	100	67	87	33	40	67	40	80	67
Inherited 2 sides strong	33.9	7	93	80	73	**80**	93	100	93	87	80	73	100	100	100	93

FIGURE 42.

matism or neuritis; to which I will reply that we have excluded nearly half of the records taken because the patients did not know sufficient detail regarding these facts; and also, that if the cause of the parent's death was sufficiently impressed upon the minds of the patients that they could say clearly that it was from Bright's disease or heart, etc., they were generally correct, which we have determined by making a large number of verifications by communications with family physicians. I would also emphasize that since if the patient did not feel sure no entry was made, the effect on the record would be that the individual in question was clear and the total effect would be to make the case less strong than it should be rather than more strong than it should be. If then our percentages seem high with incomplete records, we are very sure that they would be much higher if we had complete records in all cases. That this is true, we have demonstrated to our satisfaction by establishing groups where we were able to get very complete records for all or most of the individuals involved, and in those cases, as will be shown presently, the percentages are very much higher.

We selected fifteen families in each of the following groups: non-susceptibility or absent, acquired susceptibility, inherited susceptibility one side mild, inherited susceptibility both sides

PTIBILITY GROUPS

Average No. of Lesions in Family									Local Expressions of Dental Infections					
Tonsils	Rheumatism	Heart	Neck	Nerves	Internal Organs	Special Tissues	Total Severe	Total Severe and Mild	Caries	Pyorrhea	Open	Locked	Rarefying	Condensing
1.08	2.48	1.35	1.01	5.37	3.12	1.94	11.34	16.35	75	23	25	75	32	26
.27	.47	.13	.13	.47	.47	.13	**1.07**	**2.07**	40	40	40	60	67	0
.40	.73	.27	.60	2.47	.93	1.00	**4.20**	**6.40**	80	33	33	87	33	20
.80	3.00	.87	1.20	4.40	1.87	1.27	**9.60**	**13.40**	67	33	40	87	33	20
1.40	4.07	1.93	1.27	6.13	3.73	2.00	**15.30**	**20.53**	93	20	27	80	40	33
1.07	3.40	2.00	1.80	7.00	5.20	2.07	**17.20**	**22.53**	80	20	20	80	27	33
3.13	7.07	5.13	3.33	16.93	7.07	7.60	**32.20**	**50.27**	93	0	0	87	7	67

mild, inherited susceptibility one side strong, and inherited susceptibility both sides strong. The figures for these groups are shown in Figure 42, from which it will be noted in the last two columns under "Average No. of Lesions in Family" that the total severe rheumatic group lesions per family in the non-susceptibility or absent group is reduced to 1.07, and the severe and mild rheumatic group lesions to 2.07; the group with acquired susceptibility, severe lesions, 4.2 severe and mild lesions 6.4; inherited susceptibility, mild one side of ancestry, severe 9.6, severe and mild 13.4; inherited both sides mild, severe 15.3, severe and mild lesions 20.5; inherited one side strong, severe lesions 17.2, severe and mild lesions 22.53; inherited two sides strong, severe lesions 32.2, severe and mild lesions 50.27.

The above is an analysis of the ancestry on the premise of the patient's condition. When we reverse this and use the ancestry as the basis on which to judge the progeny, results are quite as striking, as shown in Figure 43; from which it will be seen that in eight families with an average of 7.3 children per family with no apparent susceptibility, the average number of children affected per family was .63; which means that during the entire lifetime up to the time of the record less than one child per family had shown at any time a rheumatic group lesion. The percentage

MENDELIAN FACTORS

Relative number of children affected in families when
(a) Patient has *absent* susceptibility.
(b) Patient has *acquired* susceptibility.
(c) Patient has *strongly inherited* susceptibility.

	No. of cases	Average No. of children per family	Average No. of children per family affected	Percent of children affected	
(a)	8	7.3	0.63	9%...........	**Susceptibility absent**
(b)	8	7.2	1.2	17%...........	**" acquired**
(c)	8	9.0	4.0	44%...........	**" inherited**

FIGURE 43.

A PROGRESSIVE STUDY OF THE RELATION OF THE SUSCEPTIBILITY FACTOR OF INDIVIDUAL PATIENTS TO THAT OF THEIR RELATIVES.

	Group	No. of Families in Group	Average Total Severe Rheumatic Lesions per Family	(Applied Mendelism)						
				Average No. of Individuals Per Family Who Have Had Lesions In:				Percentage of Individuals with:		
				Joints & Muscles (Rheumatism)	Nerve Tissues	Heart	Digestive Tract and Kidney	Extensive Caries	Locked Dental Infection	Periodontoclasia
1	Dental Patients with *No* Developed Susceptibility	35	3.7	1.1	1.0	0.5	1.0	51%	58%	23%
2	Dental Patients with an Apparently *Acquired* Susceptibility	12	4.7	1.3	1.3	0.6	1.6	91%	75%	33%
		27	7.7	2.2	2.0	1.2	2.2	78%	48%	26%
3	Dental Patients with a Susceptibility and with one or both Parents acting as *Carriers Only*	16	10.0	3.8	2.3	1.9	2.3	81%	44%	25%
4	Dental Patients with a Susceptibility and with only *One Side of Ancestry,* including the Parent Involved	8	13.6	5.2	3.4	3.3	2.1	88%	75%	0
5	Dental Patients with a Susceptibility and with *Both Sides of Ancestry,* including Both Parents Involved	7	37	12.4	8.0	9.0	7.0	100%	86%	0

FIGURE 44.

of all the children affected in this group was 9. In the second series of eight families with an average number of children per family of 7.2, where there was what we have termed an acquired susceptibility, the average number of children affected per family was 1.2, or a total for this group of 17%. In a third group of eight families with an average number of children per family of 9, the average number of children affected per family was 4, and the percentage of affected children in this group jumps to 44.

Realizing how critical one must be of his findings when searching for fundamental new truths because of the danger of seeing the thing one is looking for, I have made or have had made several separate and independent studies for the purpose of checking one against the other. The individual compiling the last group of 681 selected cases not only did not know the content of the previous compilation, but did not even know that one had been made. She was kept in ignorance of this fact for her own protection, and it is exceedingly important to find that in several particulars those records analyzed in 1919 furnish totals which are strikingly similar to those recently completed. (1922)

Figure 44 shows an analysis of five different groups slightly differently selected as follows: Group No. 1, Dental patients with no developed rheumatic group susceptibility; Group No. 2, Dental patients with an apparently acquired susceptibility; Group No. 3, Dental patients with a susceptibility, and with one or both parents acting as carriers only (parents' ancestry involved, but parents not yet); Group No. 4, Dental patients with susceptibility with only one side of the ancestry, including that parent, involved; Group No. 5, Dental patients with a susceptibility, and with both sides of the ancestry, including both parents, involved.

Among the many similarities, note that in the first group of 35 non-susceptibles the average total severe rheumatic group lesions per family is 3.7; whereas, in the recent analysis of 102 non-susceptibles, this is shown to be 4.2; (See Figure 41) and in Figure 42, the 15 strongly absent cases, 1.07. [See column "Total Severe" under "Average No. of Lesions in Family."] The corresponding groups of acquired susceptibles in these three studies show in the figures of 1919 (Figure 44) 4.7 severe lesions and in Figure 42, 4.2 severe. Groups 3 and 4 of Figure 44 are not exactly comparable to groups 3, 4, and 5 of Figure 42, though quite similar in classification of individuals. Group 3, Figure 44,

A STUDY OF SUSCEPTIBILITY OF VARIOUS GROUPS OF PATIENTS WITH RHEUMATIC LESIONS WHICH ARE APPARENTLY RELATED TO DENTAL FOCAL INFECTIONS

Group	No. of Families in Group	Age Range	Average Age	Average Total Severe Rheumatic Lesions per Family	Percentage of Patients in Group Who Have Had Lesions In:				Average No. of Individuals Per Family Who Have Had Lesions In:			
					Joints & Muscles (Rheumatism)	Nerve Tissues	Heart	Digestive Tract and Kidney	Joints & Muscles (Rheumatism)	Nerve Tissues	Heart	Digestive Tract and Kidney
1 Dental Patients with *No* Developed Susceptibility	35	19 to 85	46	**3.7**	0	0	0	0	**1.1**	**1.0**	**0.5**	**1.0**
2 Dental Patients with *Rheumatism* Most Dominant in Patient and Family	14	17 to 55	40	**14.8**	100%	95%	36%	79%	**6.9**	**2.8**	**2.0**	**3.3**
3 Dental Patients with *Nerve Lesions* Most Dominant in Patient and Family	3	31 to 42	35	**16.0**	67%	100%	33%	100%	**4.3**	**6.0**	**3.3**	**3.0**
4 Dental Patients with Lesions in *Digestive Tract and Kidney* Most Dominant in Patient and Family	8	12 to 56	40	**17.4**	50%	88%	50%	100%	**4.1**	**2.9**	**3.3**	**7.3**
5 Dental Patients with Lesions of *Rheumatism and Nerves* Most Dominant in Patient and Family	9	26 to 63	44	**18.3**	100%	100%	44%	78%	**6.4**	**5.7**	**2.6**	**3.7**
6 *Appendix Infections* in Children and Grandchildren where Lesion was Dominant in One Side of Ancestry	3	12 to 48	31	**22.0** (**23.3**)x	67%	67%	67%	100%	**6.0** (**8.3**	**4.0** **4.0**	**3.3** **3.3**	**8.7** **9.7**)x
7 Dental Patients with Lesions of Rheumatism and Heart Most Dominant in Patient and Family	14	18	42	**24.0**	100%	93%	**100%**	71%	**7.4**	**4.4**	**6.9**	**3.5**
8 Dental Patients with *Heart Lesions* Dominant in Patient and Family	7	30	43	**28.2**	71%	86%	**100%**	86%	**7.0**	**6.1**	**9.7**	**5.0**
9 Dental Patients with *Rheumatism, Nerves, Digestive Tract and Kidney* Most Dominant in Patient and Family	6	21	35	**27.8**	100%	100%	50%	100%	**9.2**	**7.7**	**3.7**	**7.7**

x—Children included.

FIGURE 45.

has severe rheumatic group lesions 10 per family, and Group 3, Figure 42, has 9.6; Group 4, Figure 44, 13.6, Groups 4 and 5, Figure 42, 15.3 and 17.2 respectively; Figure 44, Group 5, strong inherited susceptibility from both sides, 37, and Figure 42, Group 6, similar strong inheritance, 32.2.

Similarly, Figure 45 made in 1919, in which the dominance in its relation to the particular type of tissue is involved, shows progressively percentages beginning with 3.7 for non-susceptibility and increasing to 27.8 for susceptibility to lesions in several types of tissues. The average total severe rheumatic group lesions per family for the group with absent susceptibility, marked "No Susceptibility," is 3.7; those with rheumatism the most dominant in the patient and family, 14.8; nerve lesions most dominant in patient and family, 16; digestive tract and kidney, 17.4; a combination of muscle and nerve involvements as rheumatism and neuritis, 18; appendix infections where lesion was dominant in one side of the ancestry, 22; where rheumatism and heart affections were both expressed in the family, 24; heart affections alone dominant in the family 28.2; and where a combination of affections as rheumatism, nerves, digestive tract, and kidney, were all dominant in the family, 27.8.

A further comparison of data developed in the two series of studies is of value. At that time one hundred consecutive families were studied (See Figure 46) and the ratios of lesions in various types of tissue recorded for comparison. The recent analysis (1922) of seven hundred cases (See Figure 41) selected from dental practice (as distinguished from individuals studied under other conditions to be discussed later), when compared with the former determinations of 1919, reveals the following remarkable similarity of figures: Joints and muscles, former, Figure 45, 65%, recent, Figure 41, 63%; Nerves, former 70%, recent 81% (we are recognizing more nerve lesions than formerly with increased information); Heart, former 28%, recent 26%; Internal Organs, former 61%, recent 60%; Tonsils, former 62%, recent 53%.

A comparison of the severity and frequency of lesions in the two sexes, when compared in the two sheets of studies, again repeats an important similarity. In the former studies of one hundred patients with severe lesions, 75% were females and 25% were males; and in the recent study of 681 cases, 71% were females and 29% were males. In this connection, it is interesting

COMPARISONS OF TWO SEPARATE STUDIES

Relative Prevalence of the Following Lesions in Affected Patients

Summary Made In	No. of Affected Patients	Joints and Muscles (Rheumatism)	Nerves	Heart	Internal Organs	Tonsils
1919	100	65%	70%	28%	61%	62%
1922	681	63%	81%	26%	60%	53%

FIGURE 46.

DOMINANCE OF SPECIAL TISSUE LESION IN BOTH PATIENTS AND FAMILIES (TEN)

Group	No. of Males	No. of Females	No. of Lesions in Ten Patients							No. of Lesions in Families									Local Expressions of Dental Infections					
																	Total							
			Tonsils	Rheumatism	Heart	Neck	Nerves	Internal Organs	Special Tissues	Tonsils	Rheumatism	Heart	Neck	Nerves	Internal Organs	Special Tissues	Severe	Severe & Mild	Caries	Periodontoclasia	Open	Locked	Rarefying	Condensing
Rheumatism	2	8	5	**10**	2	6	4	4	3	8	**59**	7	9	19	19	10	104	131	9	1	1	6	2	3
Heart	3	7	7	6	**10**	5	7	3	8	12	24	**57**	6	25	13	19	121	156	10	1	2	8	3	5
Nerves	2	8	5	6	2	7	**10**	7	7	10	15	9	10	**142**	28	19	180	233	9	3	3	9	5	5
Internal Organs	2	8	6	4	0	6	9	**10**	6	6	13	9	10	30	**90**	12	136	170	7	3	3	7	4	3

* Type of susceptibility—inherited.

FIGURE 47.

MENDELIAN FACTORS

Cases	Average No. of children per family	Average No. of children affected	Fathers affected	Fathers' Relatives affected	Mothers affected	Mothers' Relatives affected	Dominance in ancestry	Dominance in children	Mendelism
42	5	2.7	76%	61%	50%	55%	61%	54%	88%

FIGURE 48.

to note that in the progressive classification of cases from absence of susceptibility through mild to severe, the ratio of males to females keeps changing in a definite and geometric proportion; whereas, in the group Figure 42 of absent susceptibility, the ratio of males to females in the cases selected at random was 53% males to 47% females; acquired susceptibility, 40% males and 60% females; inherited susceptibility, mild one side only, 33% males and 67% females; inherited strong one side, 27% males and 73% females; inherited two sides mild, 20% males and 80% females; inherited two sides strong, 7% males and 93% females. This last group represents persons with very severe lesions. (This tells a tragic story which is discussed later in the chapter on Overloads and is largely a record of the terrific charge that Nature has made against motherhood.)

An analysis of these data throws a very important new light on the nature of an inherited susceptibility, which is augmented by careful application of these observations in clinical practice. We have thought of susceptibility in terms of a systemic defense. After we make an analysis, for example, of hearts in 681 selected cases, consecutive except that there have been eliminated all cases in which we could not secure a sufficiently complete record, in these we find that 26% of the patients, approximately 1 in 4, have some heart disturbance. This in itself is a tragic revelation, especially when we contemplate that 1 in 10 of the deaths of all ages in modern civilized communities is from heart affection. An examination of the heart column in Figure 42 shows a progressive column of ratios of patients with heart involvements; from 0 in Group 1, those without streptococcal susceptibility, 20% in the acquired group, 13% inherited one side mild, 27% inherited one side strong, 40% inherited two sides mild, to 80% inherited two sides strong. Comparing this with the data in Figure 45 under the column "Percentage of patients in group who have had lesions in various tissues," we find that the percentage starting in Group 1 as 0, advances progressively so that in the group in which the heart was dominant in the family, in seven families which were studied at that time, and many more of which have been added, the ratio is 100%. While these were unusually severe instances of susceptibility to heart lesion, it is most striking to see how frequently the susceptibility to heart is dominant throughout the family with complete absence of other rheumatic group lesions; and, similarly, kidney, muscles and joints, digestive tract, and special tissues, each dominant in the particular family group while all other tissues remain very low or completely absent. This is strikingly revealed in a section of Figure 42 entitled "Average No. of Lesions in Family" and in Figures 43 and 44, and in the totals of Figure 41. It is, however, true, as revealed in all of the charts, that the heart or some other tissue may be dominant by inheritance and there may be an acquired susceptibility for some other tissue, which other tissue is in the majority of cases the nervous system.

Contrary to our expectations, we do not find that the inheritance of a susceptibility to rheumatism necessarily carried with it a susceptibility to heart or *vice versa*. This is strikingly illustrated in Figure 47 which shows many instances of heart's being dominant in the family and no rheumatism; and likewise, rheumatism dominant in the family and no cases of heart. In a study of the relation of other infections, such as syphilis, to heart involvements we show that this is an important factor as a source of heart lesions and that these individuals frequently, if not generally, have distinctive characteristics aside from their history and Wasserman reactions. The data in the chart in Figure 47 is exceedingly important because it shows that in forty selected families where the chief lesion of the patients studied was one of the four following—rheumatism, heart, nerves, or internal organs—in every instance that lesion by far outnumbered all others in the individuals constituting the patients' relatives, as, for example, in ten patients affected the number of instances of rheumatism in other members of the family was 59, whereas no other lesion of the rheumatic group exceeded 19. Where heart was the chief lesion of the patient there were 57 cases of heart in the immediate family and no other lesion exceeded 25. Where nerve lesions were the chief lesions in the patient there were 142 instances of severe nerve lesions in the family, whereas no other lesion exceeded 28; and where the lesion of the patient was in the internal organs there were 90 instances of lesions in the internal organs of other members of the family, whereas no other tissue exceeded 30.

When we take the total number of heart cases in 681 family groups, we find it to be 916 hearts, or an average of 1.35 per family. An actual count of the families having at least one case of heart reveals that of the 681 families, only 413 have any heart lesions, an average of 2.2 per family; and of these, 100 families had over half of the lesions. An analysis of the families included in Figure 42 shows that in each of the six groups of fifteen families each, there is not an instance where the patient being studied had developed a heart lesion, where there was not a record of a heart lesion in the brothers or sisters, or fathers' and mothers' families; and in practically all instances where the number of hearts per family group is greater than the average for the entire group, the patient is recorded as having a heart lesion, and the severity of the heart lesion is in striking proportion to the dominance of the lesion in the family. The groups of fifteen in Figure 42 show more striking conditions than the average. Similarly and quite as strikingly, we might study kidney, joint tissues, and other tissues, though not necessarily the nerve tissues which apparently may have a susceptibility by inheritance or be an acquired factor.

An analysis of the data has been made to see the evidence of mendelism. This is shown in Figure 48. In 42 cases of marked susceptibility, the average number of children per family was 5. The average number of children affected was 2.7, which you will note is 54%. In these 42 families, 61% of the two ancestral families had been afflicted with severe rheumatic group lesions. The dominance, therefore, will be seen to be 88% of that in the preceding generations, which we may take as a factor of mendelism.

It will be of interest to note the relation of inherited susceptibility to both the mothers' and the fathers' sides of the ancestry. In the patients, 73% showed inheritance of the chief severe lesion, and 27% an acquired susceptibility. Of the inherited, 44% were singly, that is from one ancestral branch; only 29% from both sides of the ancestry. Of the singly inherited, 23% showed inheritance through the maternal side, and 21% through the paternal side.

Where the susceptibility was apparently an inheritance quality, we found that in involvements of joints and muscles, there were 4 males to 5 females; nerve tissues, 2 males to 3 females; heart, 3 males to 4 females; digestive tract and kidney, 4 males to 5 females; nervous system, 3 males to 5 females; making a general average of 3 males to 4 females. One of the most striking results of this study has been to find that when an *acquired susceptibility* obtains—in other words, where the individual with normally an ample defense has been overloaded—in the great majority of individuals the break came in the nervous system. Overloaded tissues in general tend to break and become a prey to streptococcal infection or toxic irritation.

Reading downward in most of the columns of the various charts you will see evidences of a progression, some of which are very striking. We shall later discuss in Chapter 21 the forces which tend to make tissues susceptible, which are not limited to inheritance but have to do with injury and overload of various types. This extensive study of the characteristics and relationships between systemic involvements and individual susceptibilities has brought out many other very striking new facts, such as the type of the tissue reaction about apical involvements in relation to the systemic susceptibilities, the relationships of susceptibilities to dental caries and periodontoclasia (pyorrhea alveolaris), which have been made the subjects of special researches and will be discussed in this order in the three succeeding chapters.

SUMMARY AND INTERPRETATION.

To summarize:

(1) The evidence that we have secured to date on the problem of the variations in susceptibility, while not sufficient for a final statement, is ample to suggest what will be a much safer interpretation until further data are available. To recapitulate briefly, individuals instead of being similar and therefore comparable in their susceptibilities to infection, divide themselves into three groups: Non-susceptibles, acquired susceptibles, and inherited susceptibles.

(2) The tendency of an individual to develop both general and special systemic involvements has a direct relation with, and proportion to, the susceptibility of the various members of that family circle.

We would therefore restate the fourth fundamental as follows:

Individuals as a whole do not react sufficiently similarly to justify the premise that they could all be judged by the same standards and therefore be considered comparable; that individuals can be classified into groups, the members of which are sufficiently similar to be judged by the same general standards, and they may therefore be considered comparable.

CHAPTER V.

RELATIONSHIPS BETWEEN LOCAL AND SYSTEMIC REACTIONS.

PROBLEM: Is it true, as generally presumed, that there are no distinguishing characteristics which relate the type of local periapical reaction to the nature and extent of systemic reaction?

INTRODUCTION.

Problem No. 3 was a study of the local characteristics of the periapical lesions as they develop in various individuals, and revealed (a) that infection may or may not produce extensive absorption in bone, and (b) that a given or similar dental infection will not necessarily express itself in the local tissues of the mouth approximately the same in all people; that these expressions tend to be of three different types which we have as a grouping for individuals, and that the individuals of this group therefore are comparable in this regard. The differentiating characteristic of these three groups was that the first had very extensive absorption of alveolar bone about the apex of an infected tooth, a marked rarefying osteitis; the second was similar except that it tended to have a zone of condensing osteitis surrounding the zone of rarefying osteitis; and the third with a similar quantity of infection had a relatively limited area of rarefying osteitis frequently surrounded by a condensing osteitis.

Problem No. 4, Chapter 4, was an analysis of the presumption that all individuals are comparable. The research data strongly indicated that they are not; that while there is a variation through a wide range, that variation still permits of individuals' being roughly grouped into three general classes with regard to the presence or absence of systemic lesions of the types which we have classified as the rheumatic group affections frequently, if not generally, produced by streptococcal invasion.

This research, which we have designated as Problem No. 5, is a study to determine whether or not there is a relationship between the groupings disclosed in the researches of these last two chapters. This problem may then be stated briefly as "The Relationships between Local and Systemic Reactions".

EXPERIMENTAL AND DISCUSSION.

Since, according to the presumption, all individuals are similar, and since dental infections are entirely dependent for their characteristics upon the type of organism which has chanced to secure access, therefore there are no characteristics of the local tissue pathology which are related to the degree of susceptibility or nature of systemic involvement. Our problem more specifically stated is "What relationship, if any, exists between the forces which make individuals group with regard to their local tissue reactions about infected teeth, to those forces which make them group with regard to their systemic involvements into absent susceptibility, acquired susceptibility, and inherited susceptibility."

In order to determine this we have made a very careful study of the local tissue reactions found about the teeth in the 1400 cases from which the 681 cases have been selected as being sufficiently complete in detail to be worthy of comparison. Our charts have been provided with spaces for recording in detail the type of dental pathology found in the various cases. In Figure 49 (also shown in Figure 42 of Chapter 4) there is a progressive increase in the dominance of rheumatic group lesions with the dominance of the inheritance, heart lesions, for example increasing from 0 to 80 per cent, and lesions of other tissues increasing in about the same proportion. The last division shows under "Local Expressions of Dental Infections" that open dental infections, by which we mean those that have a communication with the mouth cavity, were found present in 40 per cent of the individuals of the absent group, 33 per cent of the acquired group, 40 per cent inherited one side mild, 27 per cent inherited two sides mild, 20 per cent inherited one side strong, and 0 inherited two sides strong. Locked infections increase through these groups from 60 per cent to 87 per cent. Rarefying osteitis decreases from 67 per cent in the class of absent susceptibility to 7 per cent in the inherited susceptibility two sides strong. Condensing osteitis is present in 0 per cent of cases of the class of absent susceptibility and increases progressively to 67 per cent inherited two sides strong. It is significant that the individuals making these figures had not the slightest conception of what they were for or what information was going to be developed.

The significance of this important new truth cannot be realized suddenly. It is only by seeing patient after patient of these

RELATION OF LOCAL STRUCTURAL CHANGES TO SYSTEMIC SUSCEPTIBILITY

Susceptibility Class	Age	M	F	Tonsils	Rheumatism	Heart	Neck	Nerves	Internal Organs	Special Tissues	Open	Locked	Rarefying	Condensing
Groups of 15														
Absent	40.7	53	47	27	13	0	13	13	7	7	40	60	67	0
Acquired	47.9	40	60	40	47	20	53	87	53	53	33	87	33	20
Inherited 1 side mild	43.4	33	67	53	93	13	60	80	47	47	40	87	33	20
Inherited 2 sides mild	40.9	20	80	60	87	40	73	80	67	73	27	80	40	33
Inherited 1 side strong	39.4	27	73	47	93	27	80	100	67	87	20	80	27	33
Inherited 2 sides strong	33.9	7	93	80	73	80	93	100	93	87	0	87	7	67

FIGURE 49.

various classes and observing how constantly the local reaction about the teeth corresponds with phases of the systemic susceptibility to rheumatic group lesions that one visualizes its full significance. When we compare these data with the charts shown in Figures 38, 39, and 40, of Chapter No. 3, we find that the individuals whose cases were found to be typical of the type of structural change which we have represented in Figure 38, all belong to the class which we have referred to as having absent susceptibility. The structural change in alveolar bone about infected teeth of this group is that of an extensive alveolar absorption as a rarefying osteitis diffusing into the medullary spaces without condensing osteitis. The group represented in Figure 39 corresponds and is, we find, the same group of individuals that make up our lists, when studied from the standpoint of systemic involvement, of those of acquired susceptibility. They have evidence of an extensive rarefying osteitis surrounded by a zone of condensing osteitis, sometimes thin, sometimes of considerable depth. And, similarly, the group which we have expressed in Figure 40 as having a very limited zone of rarefying osteitis in comparison with the quantity of infection, surrounded by a blurring of the medullary spaces or with a condensing osteitis diffusing into a general bone condensation, corresponds with the group of strongly inherited susceptibility to rheumatic group lesions.

To be more specific, Figure 50 shows the condition in the mouth (as revealed by the roentgenograms of two individuals from each of the following groups: A and B, absent susceptibility; C and D, acquired susceptibility; E and F, mildly inherited susceptibility; G and H, strongly inherited susceptibility;) to be as follows: There is very extensive alveolar destruction about infected roots, particularly the first molar. This includes also a marked tendency to root absorption, with the result that the mesial root of the molar is practically obliterated. There was a fistula over each one of these three teeth, with exudate oozing on compression. This man, fifty-two years of age, was physically in excellent condition with but one exception: limitation of the use of his eyes in reading, not sufficient to produce lesions but requiring glasses. After the removal of his dental infections which were extensive, he found he could read without limitation and that without his glasses. Not only was his system excellent and free from rheumatic group lesions notwithstanding this abundant infection, but he had seven brothers no one of whom had ever suffered from any of the rheumatic group lesions, and three sisters none of whom had suffered from any of the rheumatic group lesions. A study of his father and the father's brothers and sisters, and the mother and her brothers and sisters, reveals but one mild instance of a suspected rheumatic group lesion on either side of the ancestry, including the grandparents on both sides. This is clearly a case of absent susceptibility.

In Figure 50-B showing extensive alveolar absorption about the apices of the roots of a molar and bicuspid, we have a condition in the mouth of a man of twenty-five years of age. Note the extensive absorption of bone and tendency to absorption of root ends. Physically, this man has scarcely known a limitation. Material aspirated from an apical area showed many giant cells, which particular cell we have only found in cases of very high defense where there is absorption of root apices. His physical classification is also absent susceptibility. His family history is as follows: He has not had during his lifetime a single break of the rheumatic group lesions. His brother and four sisters have also been entirely free. His father is fifty years of age and has not had a symptom of any of the rheumatic group lesions, nor have any of the father's three brothers or two sisters, his father's

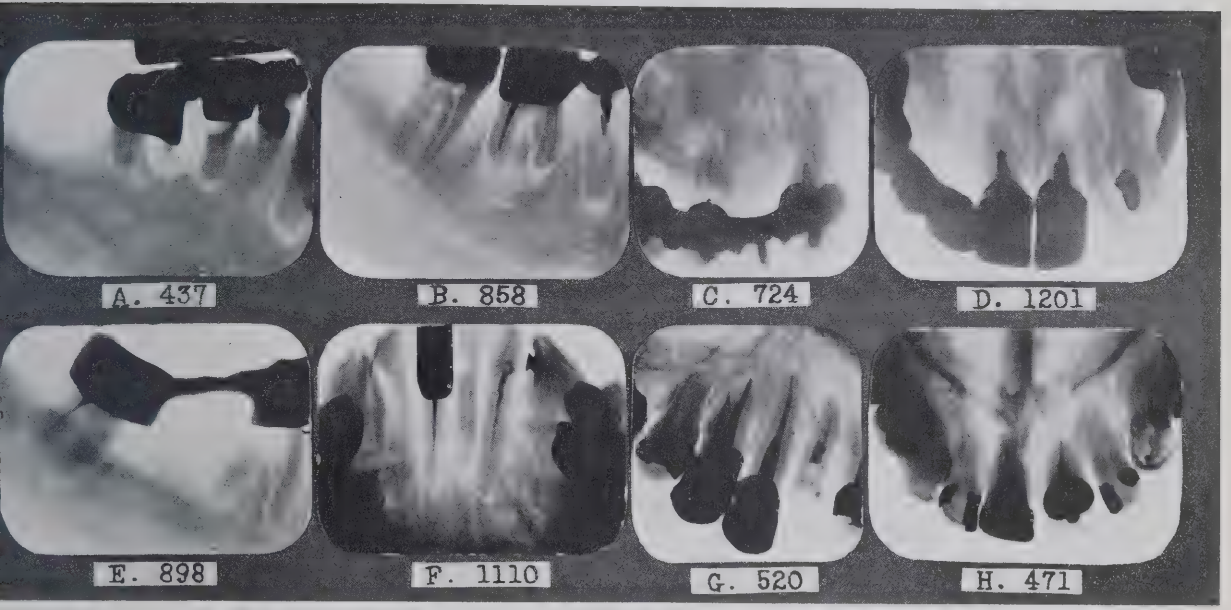


FIGURE 50. TYPICAL ILLUSTRATIONS OF THE LOCAL REACTIONS IN THE DIFFERENT GROUPS.

father and mother living to ninety years of age each. His mother at fifty-two years of age has had hardening of the arteries and her father had some rheumatism. Otherwise the record is perfectly clear on the mother's side. The mother's mother is living and very strong at seventy-five.

In Figure 50-C we have a patient with very extensive absorption of alveolar bone but with a zone of condensed bone surrounding the immediate zone of rarefaction at the apex and about the bicuspid root. This patient has been free from rheumatic group lesions during his lifetime until recently when he has developed neuritis. He is sixty-seven years of age, has had five brothers and six sisters, one of the latter being ninety years of age. His father died of typhoid at fifty-eight and his father's father and mother both lived to ninety. His mother died at ninety-two and her mother at ninety-two. There has not been a single case of rheumatic group lesion on either side of the ancestry. This man's classification is clearly one of an acquired susceptibility.

In Figure 50-D we see the local dental expression to be one of quite extensive alveolar absorption above the right central which shows a record of condensing osteitis surrounding the rarefying. Physically, the patient presented with pain of recent development in his right shoulder and right knee. He has had three brothers and three sisters. One of the former has had a heart involvement.

Otherwise the brothers and sisters have been free from rheumatic group lesions. His father died at sixty of a stroke and the father's side of the ancestry with three brothers and three sisters was free from rheumatic group lesions, his father's mother dying at eighty-five. The patient's mother is living at seventy-seven, is in excellent health, and has never been ill except one attack of pneumonia and some asthma. His mother's father died at eighty and her mother at eighty-nine, and these with her four brothers and six sisters were entirely free from rheumatic group lesions. There is a possibility that the heart involvement of his brother, though not accompanied by rheumatism, may have had some relation to his own rheumatic development, but we assume not since there is no evidence of it elsewhere in the family. We would therefore classify this as one of an acquired susceptibility.

In Figure 50-E the dental pathology as revealed in this case shows much less absorption of the alveolar bone surrounding an apparently unfilled root, there being no root filling in the mesial canal of the third molar and not as extensive absorption about the roots of the first molar as we should expect. A study of this patient's susceptibility reveals that he has had mild attacks of rheumatism and some slight evidence of neuritis. He has one sister. She has had mild rheumatism. His father died at seventy of anemia and has a history of mild rheumatism. His father's father died at seventy-six of kidney and heart involvement, probably related to the rheumatic susceptibility; his father's mother at eighty-six with a definite history of rheumatism. His mother is living at seventy-six with a definite history of rheumatism and gall-stones. The mother's mother had heart and kidney involvement and the mother's sister very severe rheumatism and heart involvement. There has therefore been a very definite tendency to rheumatism in this family; and while it has been on both sides, neither of the parents has suffered severely. We would therefore record it as a mildly inherited susceptibility.

Figure 50-F shows three lower incisors, one of which has a putrescent pulp without root filling, yet neither it nor the adjoining teeth show extensive absorption. This patient is fifty-five years of age and presents with mild neuritis and rheumatism of recent development in his hands. Otherwise he has been entirely clear during his lifetime. His two brothers and a sister have not had disturbances. His father died at seventy-nine, having had severe attacks of rheumatism and neuritis. His father's father died at seventy-four. The patient's mother died of pneumonia at thirty-seven, the mother's father at sixty-six, the mother's mother at eighty-four, all without symptoms of rheumatic group lesions. Since there is a definite history of rheumatism and neuritis with the father, not in other members of the ancestry and not previously in the patient, we would classify this as a case of mildly inherited susceptibility.

Figure 50-G shows a lateral of a girl only twenty-three years of age. There has been a moderate absorption but no fistula and no local pain. She presents with quite severe rheumatism and severe lassitude. Even at the age of twenty-three she has had quite severe rheumatism, neuritis, nervous breakdown, and digestive disturbance. She has two brothers and four sisters. Each one of the six brothers and sisters has had rheumatism and each, like herself, has been operated for tonsils. Her brothers and sisters have also all had acute neuritis. Her father died at fifty-six, having had acute rheumatism and neuritis and acute digestive disturbance. His father died at eighty-one, having been a sufferer from rheumatism and neuritis. The father's mother had also suffered from rheumatism, neuritis, and digestive disturbance, as did also the father's brothers, three of whom and the patient had kidney involvement. The patient's mother is living at sixty-one but has suffered severely during her life from rheumatism, neuritis, and digestive disturbance. Her mother died at seventy, having suffered from these severely; and the mother's mother died at thirty-nine of acute rheumatism. The mother's brothers and sisters also suffered from rheumatism. We have, then, a family in which there have been sixteen cases of rheumatism, eight cases of acute digestive disturbance, and twelve cases of neuritis. This girl is breaking at twenty-three, not because of severe overload but in spite of the absence of severe overload. Of her two brothers and four sisters ranging in age from twenty-one to forty, everyone has similarly broken. Her father and mother began breaking seriously at about forty years of age and scarcely were free from disturbance thereafter. This girl by inheritance has an exceedingly marked susceptibility to not one but three at least of the severe rheumatic group lesions, involving muscles and joints, nerve tissues, and digestive tract tissues. We therefore record her case as one of strongly inherited susceptibility.

The dental pathology as shown in Figure 50-H is very misleading. There is very little evidence indeed of severe involvement of the root filled centrals; yet on extraction the root apices were badly discolored and therefore showed marked involvement though there was very little destruction of alveolar bone. She has presented with a very severe heart involvement and severe nervous breakdown. Her life was being despaired of. She had been troubled during that time a great deal with neuritis, nerve lesions, and heart involvement. Her age is forty-two. Her goiter has developed since the birth of her two children. She has had symptoms of rheumatism. She has had four brothers and four sisters, one brother and two sisters having had rheumatism. All four of her sisters have had severe nervous breakdowns as has also one brother. One sister has a severe heart lesion. Her father died at seventy-five of rheumatism and heart involvement. Her father's father died at forty, and three of her father's brothers and her father's sister all died of heart involvement. Her mother died of heart involvement at seventy-eight, having suffered severely from nervous breakdown and rheumatism. This patient has shown a marked susceptibility to these lesions during her lifetime, as have also her brothers and sisters and both sides of the ancestry. We would therefore classify her case as one of strongly inherited susceptibility.

If, now, we will review these four groups, we find the following: The two individuals of the first group (A and B) have never yet had any of the rheumatic group lesions notwithstanding various overloads, nor did the members of their families or their ancestries. They therefore classify readily as having an absent susceptibility. C and D had a history similar, in general, so far as they themselves and their ancestry were concerned except that they have lately broken. With each there has been a distinct physical overload of overwork. The development of their rheumatic group lesions has been a recent, though quite severe, disturbance. With the removal of the dental infections without a change in the overload of business cares, their conditions have cleared up completely and promptly. E and F are two patients who have developed acute rheumatic group lesions as rheumatism, which disturbances were definitely present in the ancestry. They are therefore classified as mildly inherited susceptibility. With removal of their dental infections they both had complete relief from their rheumatic disturbances notwithstanding they have maintained very busy business careers, which, no doubt, had contributed to their breaking. G and H are two cases of severe break with rheumatic group lesions that have tended to develop for some time, which lesions are very strongly present in the other members of the family and ancestry. They are accordingly classified as strongly inherited susceptibility. Each has shown very marked improvement with removal of the dental infections. The latter has taken up her home duties again as a mother and the management of a large home and is enjoying excellent health.

The question of prognosis in these various cases will be discussed in detail later. It will, however, readily be seen that the prognosis becomes less and less favorable for complete relief and freedom as the condition gets to be more strongly an inherited quality. This matter is discussed in detail in other chapters.

If, then, we will take a single tooth, let us say a lateral with all the infection of a putrescent pulp, and follow it through these different groups, we will see in detail the difference in the local structural pathology as well as in the physical systemic reactions. This we have done in Chapter 12 while discussing the relation of the quantity of absorption to the danger.

It is exceedingly significant that when we picked out a group of individuals expressing each of the different classes from the standpoint of a structural change about the teeth, and again made groups typically characteristic, and strongly so, of the different groups or classes on the basis of their systemic susceptibility, we were amazed to find that out of the hundreds of cases from which we had selected these few typical illustrations we not only had similar individuals but in a very many cases we had the identical individuals that had been selected to illustrate a group on the other basis of classification.

This one important new truth accounts for a very large part of the confusion amounting almost to bitter antagonism, that has existed in the medical and dental professions regarding whether or not dental infections are a serious factor in systemic involvements and degenerative diseases. It has been insisted by the group on one hand, on the basis of effect being in proportion to cause, that since the enormously large number, if not large percentage, of individuals presenting in the outpatient clinics of hospitals with the most abundant infections that could be found in any group, as evidenced by the quantity of pus flowing from broken down and decayed teeth, do not have any systemic involvements, therefore, it cannot be true that dental infections are an important causative factor in the systemic involvements. If any individuals would be affected, surely this group would be and they are not.

It now is demonstrated that the physical change about the root of the tooth is not a measure of the infection but a measure of the quantity and type of the reaction, not a factor primarily relating to the invading organism which is inside the infected tooth but a factor primarily relating to the activity of the defense of the individual; and when seen in this light, this whole confusion ceases to be a paradox and is completely intelligible. The individuals having the extensive rarefactions have an active mechanism of defense, which for them establishes an adequate quarantine immediately about the tooth. So long as that quarantine is maintained there is an extensive zone of rarefaction with little tendency to condensation of bone about this rarefying area. The vascularization is excellent. This also explains why these individuals without systemic rheumatic expressions tend continually to have alveolar fistulae. These are the individuals with absent susceptibility; but when their defense is broken from the many causes that will be shown in subsequent chapters, they take on a condition which we have termed an acquired susceptibility. Incidentally, their local defense goes down; the quarantine is not maintained; a changed reaction takes place about the tooth with the change in local defense; there is a condensing osteitis surrounding the rarefying osteitis; the quarantine not being maintained about the tooth, the warfare must take place in other parts of the body. These individuals probably now for the first time have the organism passing extensively from their dental infections through their bodies, and in a sense it is the first time the tissues of their bodies have been exposed to this infection. After the overloads are removed they will tend strongly to come back to their normal which is high; but in the third group with the inherited low defense there always has been a struggle, there never has been a normal local quarantine, teeth never have had fistulae because there was never an ample local reaction the by-product of which would have been a fluid which must have an exit, spoken of as pus from a fistula; the warfare has always had to be carried on in the various tissues of the body rather than in the specially designed and developed tissue which Nature establishes for the purpose of maintaining the quarantine about the root apex.

This group is always in danger. Their type of local reaction about their teeth has been what it has because of a lack of the capacity for a defensive reaction.

SUMMARY AND CONCLUSIONS.

The researches of this chapter have disclosed that individuals with a high systemic defense against rheumatic group lesions have also a very extensive zone of absorption about infected teeth; that with an overload these individuals tend to lose that high defense and develop the rheumatic group lesions, in which state they have less extensive absorption and a tendency to condensing osteitis surrounding the already existing rarefying osteitis; or if a new dental infection develops at and during this period, there is much less absorption of alveolar bone than that which occurred prior to the development of this acquired susceptibility; that the individuals of this group tend to come rapidly back to their high normal defense with the removal of their dental infections; that in most instances there has been a combination of dental infections plus overload. We assume that other focal infections have precisely the same relationships to their overloads.

In contrast to these two groups, all the members of which tended to belong to the absent susceptibility during the period of normal high resistance, we have found another group which we have subdivided into various degrees of inherited susceptibility, which susceptibility has been largely in proportion to the severity and dominance of the same expression in other members of the family and ancestry. The individuals of this group have had very much less alveolar absorption for a given dental infection, usually without a fistula. The teeth did not tend to become painful or tender as in the preceding groups. While there was relief from the acute systemic symptoms produced by the removal of the dental infections, there was a very marked tendency to recurrence. This group was termed those with inherited susceptibility ranging from mild to severe.

The prognosis was shown to be progressively more favorable with the absence of the inherited susceptibility factor. This new interpretation satisfactorily accounts for the clinical conditions and histories of the various types of individuals that are found in hospital clinics and private practice; and as the local defense is high, the absence of the systemic involvements prevails; and as the local defense is low, the prevalence of systemic involvements prevails. Therefore the individuals with the extensive areas of absorption with fistulae should be expected to be distinctly more safe than those with less effective local reaction, thus removing the paradox that has more than any other, or perhaps all other factors, blinded the professions to the role of dental infections in degenerative diseases.

We would therefore restate the fundamental which expresses the relation of local to systemic disturbances as follows:

> **Local dental pathology about an infected tooth has variations which make grouping and classification easily possible on this basis, which groups have a direct relationship with similar groupings that can be made on the basis of susceptibility to rheumatic group lesions. The local and systemic expressions are not only related, but are both symptoms of the same controlling forces and conditions.**

CHAPTER VI.

ARE APICAL ABSORPTION AND TOOTH INFECTION SYNONYMOUS?

PROBLEMS: Is it essentially true (a) *that a tooth without visible absorption at its apex is not infected, and* (b) *that a tooth with visible absorption at its apex is infected?*

EXPERIMENTAL AND DISCUSSION.

The entire system of dental diagnosis of today would seem to stand or fall on the correctness of these premises. This is true to so great an extent that the medical and dental professions of the country probably depend more on this one diagnostic means than all others combined. One has only to go to the ordinary diagnostic laboratory, whether that of a medical or dental roentgenologist, and observe the procedure. The patients, whether they come in with or without a letter of reference, will be assigned to a technician for making a complete or partial set of dental roentgenograms of the mouth. The roentgenologist or one of his assistants takes the films one at a time and holds them between himself and the light, in the better equipped laboratories often, so arranged as to be very comfortable and convenient with a hole in the top of the table covered by a piece of opal glass and an electric light beneath. A form is filled out as film after film is handled, and a decision is made in an instant on the basis of the above presumption that a tooth without visible absorption at its apex is not infected and that a tooth with visible absorption at its apex is infected.

Allowing ten films to each mouth, a little calculation readily suggests the amount of time that can be taken with each film. We know of several laboratories that claim to take complete sets of roentgenograms for fifty to one hundred patients a day, and have heard of laboratories reaching twice that maximum number. We would not suppose that even a skilled operator would undertake to interpret the films for more than one hundred patients per day. Assuming that the areas where teeth are absent are studied as well as the areas where teeth are present, which should be done, this operator would have to study the condition of several thousand teeth, or their sockets, a day. Assuming eight hours continuous study of this very exacting problem and two thousand teeth to be studied, it would allow less than fifteen seconds per tooth. We are not here presuming to discuss whether the decision is or is not correct, but simply the fact that some fundamental law must prevail, and be very constant, to make it possible for these dental diagnosticians to decide the fate of so many hundreds of teeth per day on such few seconds of observation of a record of their condition. There is no question but that this law is supposed to obtain: namely, that infection in a tooth will express itself as absorption at the root apex; and, conversely, that absorption at a root apex can have only one meaning: namely, dental infection.

This research has been made to verify the correctness of these premises. Figure No. 51-A shows roentgenograms of the central and lateral incisors of a young man, none of which would appear from the Roentgen-ray shadows to be infected; nor would the shade of any of them suggest that they were infected or abnormal. The testing of each tooth individually for a temperature response revealed the fact that the upper left central gives no response. A careful examination of the tooth and tissue surrounding it revealed a small fistula opposite about the middle third on the labial surface of the root. The tooth was opened; and a smear stained and examined immediately was found to contain an abundance of very small diplococci. B and C show roentgenograms from different angles of the tooth with a flexible gutta-percha point placed in the fistula. E and F show two views, one a direct and the other lateral, of the extracted tooth with its granuloma in position on the side of the root, also revealing apical absorption not revealed in the original roentgenograms. D shows a lateral roentgenogram of this tooth and discloses a very large lateral foramen which had its exit beneath the granuloma. A study of this tooth in Figure 51-A discloses a zone of condensing osteitis about the apex in the position which would usually be occupied by a zone of rarefying osteitis. In this chapter we are discussing the significance of what is apparent in the roentgenogram. It will readily be seen that a decision on the basis of what is apparent in the roentgenogram is utterly misleading in this case, for this patient had not only this serious local involvement but had also a systemic expression apparently influenced or caused by this involvement. Cultures were made under controlled conditions, all of which grew out long and short chained streptococci and diplococci in both aerobic and anaerobic conditions.

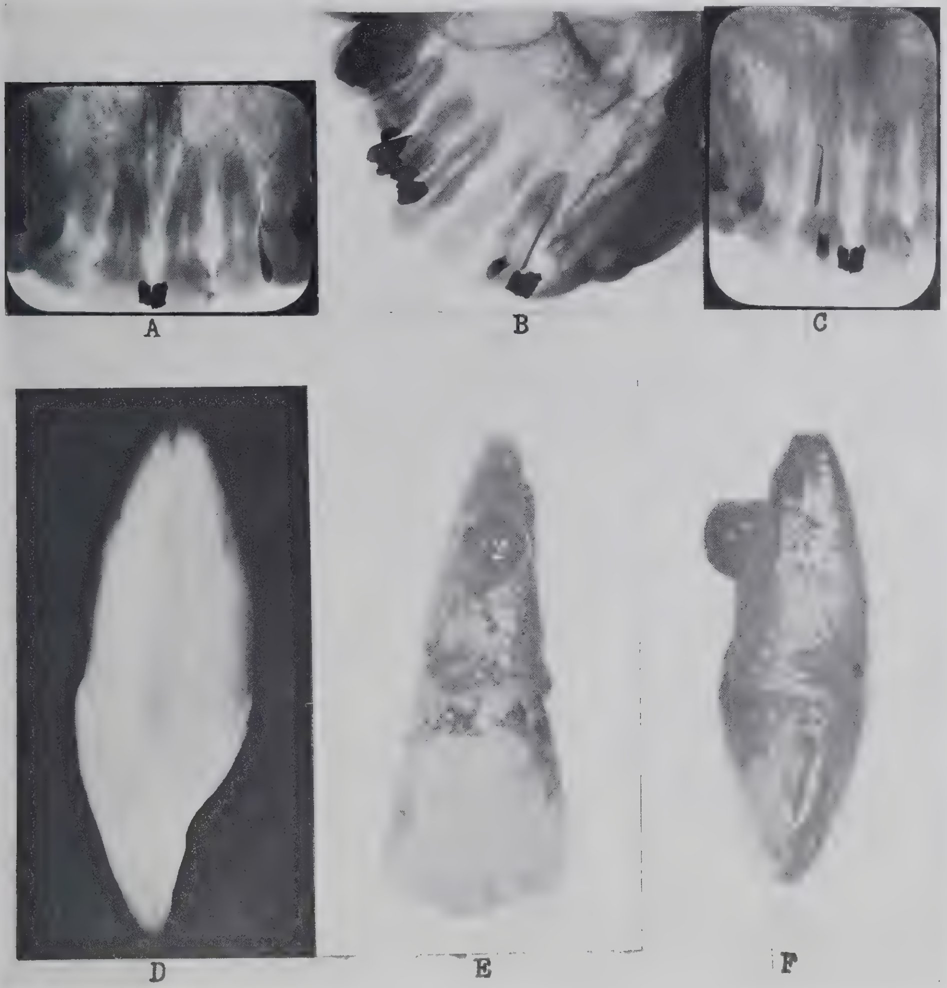


FIGURE 51. DIFFERENT VIEWS OF AN INFECTED TOOTH WHERE THE ROENTGENOGRAPHIC EVIDENCE IS NEGATIVE.

Had this lateral canal lain at right angles to the direction of the incidence of rays, the zone of rarefaction would have been on the side of the root instead of in front of or behind it, and would then probably have been disclosed. Such a case is shown in Figure 52.

Figure No. 53 shows a series of four cases of the roentgenograms of similar central incisors that have been found to be definitely and seriously infected where little or no roentgenographic evidence is apparent. In the many hundreds of cases here being reported, in more than ten per cent of instances teeth were found by other methods of study to be infected where the Roentgen-ray completely failed to reveal or even suggest that condition. To illustrate the importance of this latter we will detail the seriousness of these cases.

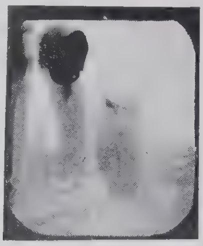
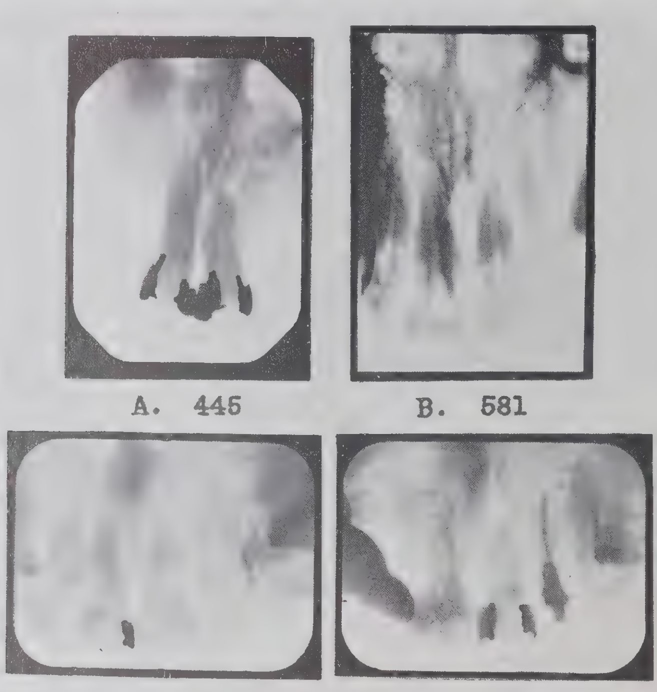


FIGURE 52. A LATERAL ABSCESS ON THE SIDE OF A BICUSPID; ALSO APICAL ABSCESS. (SEE TOOTH WITH FILLING.)



A. 445

B. 581

C. 911

D. 706

FIGURE 53. FOUR CASES WITH PUTRESCENT CENTRAL INCISORS. CONDITION NOT REVEALED ROENTGENOGRAPHICALLY.

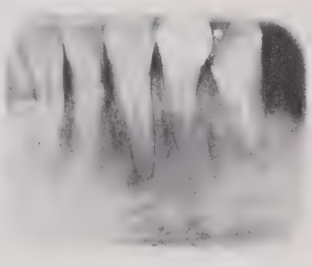


FIGURE 54. A MANDIBULAR CUSPID WITH APICAL RADIOLUCENCY BELOW A VITAL TOOTH.

A shows a woman bedridden for many months with heart and gall-bladder involvement, whose condition was so severe that her death was awaited hourly. She finally passed a large number of gall-stones after which she greatly improved, and as soon as she could be moved was brought to us for study. One of the centrals shown in A is non-vital and the seriousness of its infection was demonstrated by animal inoculation with the culture. With the removal of this and a couple of other teeth showing also a very little evidence of infection, and whatever benefit she derived from the passage of the gall-stones (which, no doubt, was very considerable) her condition has so greatly improved that for five years she has had no recurrence and is again doing her household duties with little or no evidence of heart involvement.

B shows the roentgenograms of the teeth of a young married woman, age thirty-two, who was brought to us with a heart infection. This occurred some years ago when we had more courage based on ignorance, and we consented to treat and root-fill this tooth, and make a curettage of the root end. A couple of other teeth were extracted at this time. The patient's condition improved a great deal and she resumed the responsibilities of her home. During the overload of a subsequent pregnancy her heart became very badly involved again, at which time she was carried to us; and as she lay in the ward, had so much dyspnea that about every fifth breath she would gasp. Even while lying quietly her pulse was 120. With the removal of this tooth, which (neither at the time of its first discovery and treatment or at this time, a couple of years after its root filling,) has never had any tenderness to suggest that there was anything wrong with it, the patient has had an apparently quite complete recovery, and has been taking care of her household duties, going up and down stairs, etc., for two years. She looks and feels splendid. In Chapter 60, on Circulatory System, I review this case with illustrations of the heart lesions produced in rabbits by the inoculation of the culture from this root filled and curetted tooth. The important item for us to stress is that so seriously an infected tooth gave no physical symptoms of being abnormal and, as in the last case, practically no roentgenographic evidence that it was not normal.

C shows a case of very severe rheumatism which crippled the man so severely that he could walk only by shuffling his feet

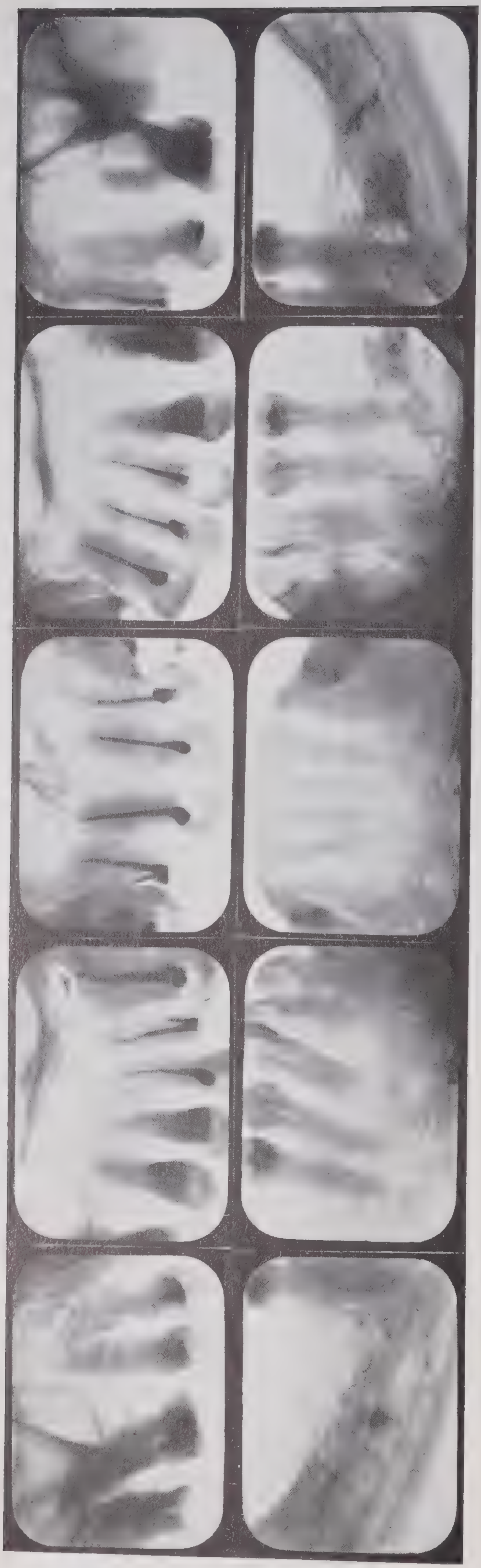


Figure 55. Maxillary anesthesia.

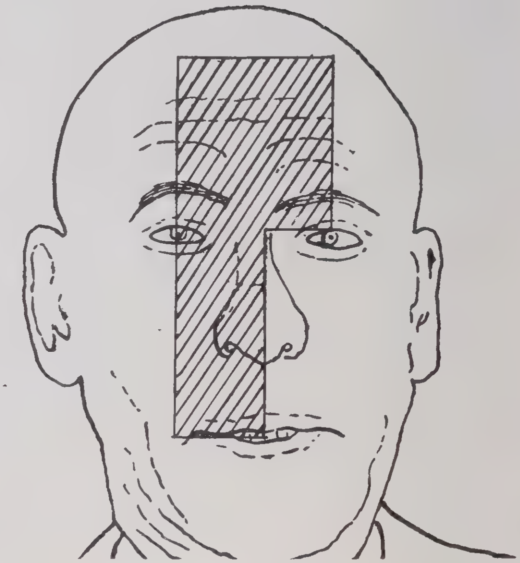


Figure 56. Showing zones of external anesthesia in the case of the previous figure.

slowly. His hands were equally helpless. With the removal of this infection his rheumatic symptoms, which had been recurring for some time, entirely and quickly disappeared and have not returned in four years. There was no change in the color of this tooth to suggest or indicate its condition and the patient vigorously protested against its removal though he is now extremely grateful. Figure 10, Chapter 1, illustrates the result of animal inoculation with this culture.

Figure 53-D shows the roentgenograms of the central incisors of a young lady suffering from a very severe neuritis in her neck. She had had a serious fall and there was a fear at one time that her neck had been broken. This pain had persisted for months though with markedly changing severity. It is not known how much of the improvement that occurred in this case was due to the removal of dental infection but there seemed to be considerable.

These are just a few typical illustrations of the extreme need for more efficient methods of dental diagnosis, than the very questionable presumption that the extent of the dental infection is that which is suggested in the roentgenogram. As shown in these four cases there was practically no evidence, for in the last case (D) the tooth that was involved was one carrying a porcelain filling, which looks like a cavity in the roentgenogram, and is not the one showing the two gold fillings and which does suggest the possibility of a periapical involvement. A close observation, however, of the involved tooth discloses a zone of condensing osteitis surrounding the apex of the upper right central.

PROBLEM NO. 5B: Does apparent absorption about a root apex necessarily reveal infection?

Figure No. 54 shows a lower left cuspid with very definite evidence of absorption of bone about the apex of the root. By both the thermal and electrical tests, and by drilling of the dentin, the tooth responds with complete normality. This tooth would readily be condemned for root filling or extraction if complete dependence is to be made upon the evidence of the roentgenogram.

Figure No. 55 shows the present condition of the upper incisors, each with areas of absorption, all of which according to history were getting larger. A careful study of the history, as furnished by the patient and the dentist, revealed the following: The woman was a colored servant in a home in another city. One day

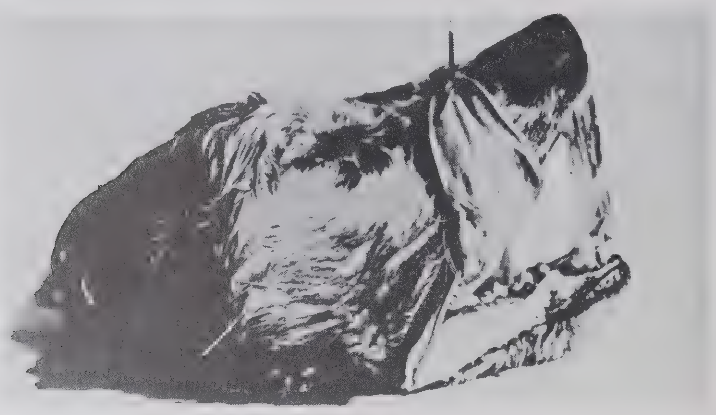


FIGURE 57 SHOWS AREAS OF ARSENICAL NECROSIS ON DOG'S TONGUE FROM DEVITALIZED TEETH.

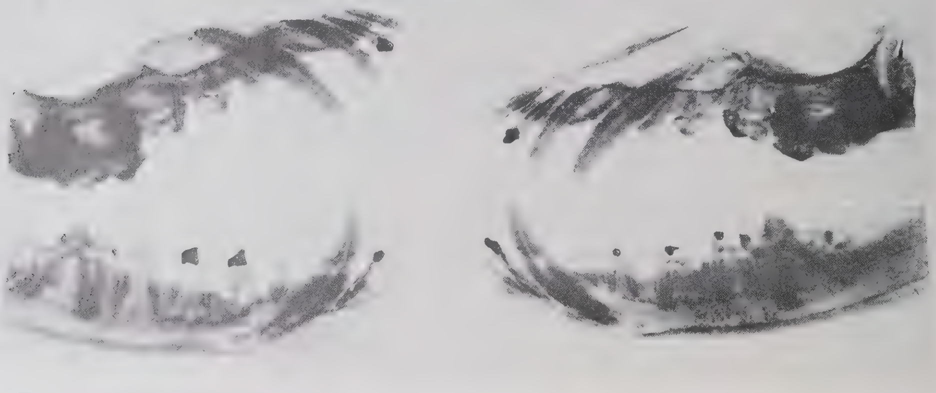


FIGURE 58 SHOWS SEVERAL VIEWS OF TREATED TEETH, SOME WITH ARSENIC, OTHERS WITH FORMALIN.

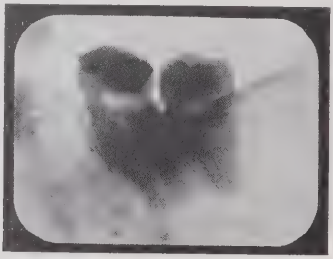


FIGURE 59. AN ENLARGED APICAL MEDULLARY SPACE RESEMBLING APICAL INVOLVEMENT.

she observed that some of her teeth felt numb when she tapped them. She went to her dentist and he tested with thermal change and by drilling, and found that the central incisors had no sensation and proceeded to remove the pulps which, as he described it to me afterwards, notwithstanding that the teeth were dead, bled like live pulps and that there was absolutely no life in them. He treated these teeth with tricresol-formalin and changed the medicine frequently. One after another, as he tested additional teeth, he found that they did not respond to temperature or to drilling, and he proceeded to remove the presumably lifeless pulps. These he also treated with tricresol-formalin and to his amazement, notwithstanding the fact that he changed the medicine very frequently, after weeks of continuous treatment he was not able to stop the apparent infection at the apices, for the abscesses, as he described them, grew larger and larger. A careful examination revealed that not only the teeth but the soft tissues of the entire upper jaw of this patient's mouth had no sensation. What had been taking place clearly was that teeth with normal pulps, but to which the nerve supply had been destroyed, had been removed, and sterile pulp chambers had been saturated with irritating medicament which penetrated the apices and produced an ever increasing zone of necrosis, and which areas were the result of irritation of a kind other than bacterial. Figure 56 shows an outline of the zones of anaesthesia. In seven years there has been little change in the boundaries of the zones of anaesthesia, though it is becoming more complete.

Figures 57 and 58 show the tongue and teeth of a dog, in whose teeth I placed arsenic and covered it carefully with amalgam fillings in cement to make a very tight seal. The dog was killed at the end of a week. The photograph shows large areas of necrosis on the tongue where the arsenic had penetrated from the pulp chamber (which is very small in dogs' teeth) through the root walls and apices to the supporting structures which were definitely necrosed and even produced extensive lesions on the dog's tongue as shown.

There was a time in the history of the practice of dentistry, and not far removed, when many dentists—we hope none now—were continually using arsenic for the devitalization of dental pulps; and I have frequently seen, when that practice was in vogue, areas of necrosis produced by the arsenic, which could easily be mistaken for zones of infection, and which could readily

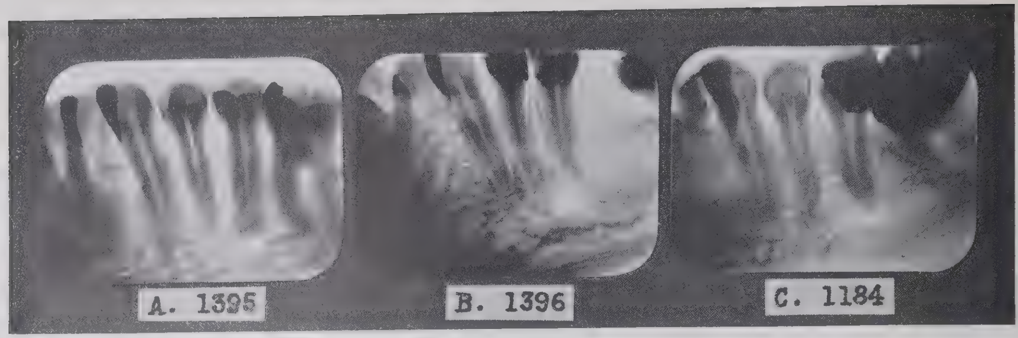


Figure 60. Mental foramina which might be mistaken for apical involvements.

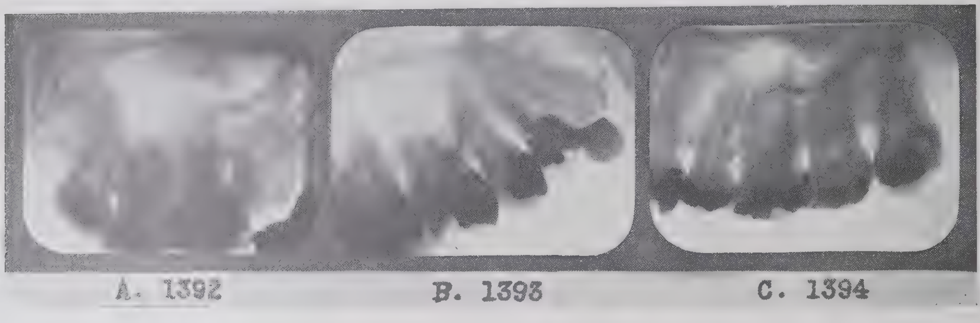


Figure 61. Anatomical relationship of maxillary sinus and palate, suggesting apical involvement.

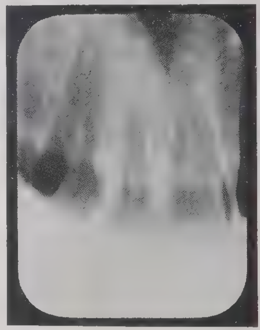


Figure 63. Thickening of peridental membrane, due to orthodontia.

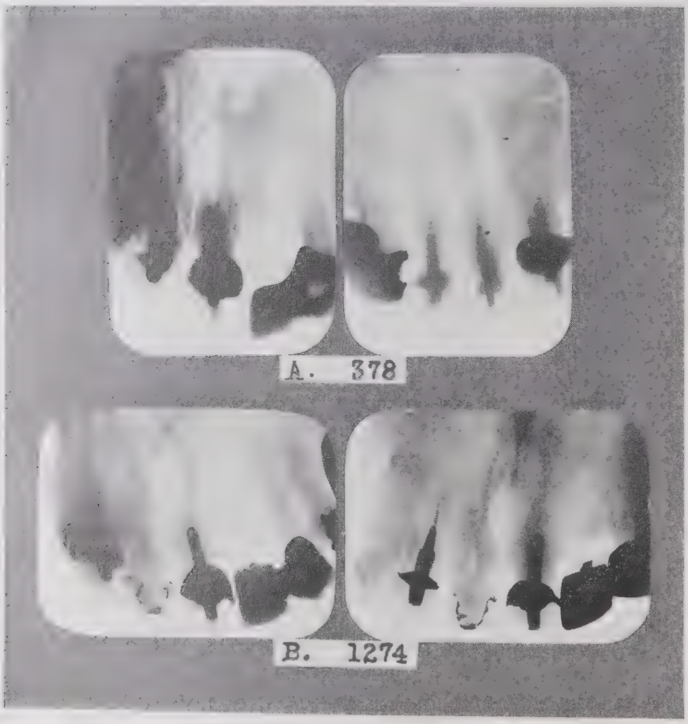


Figure 62. Two views of nasopalatine foramina, easily mistaken in one view for apical involvement.

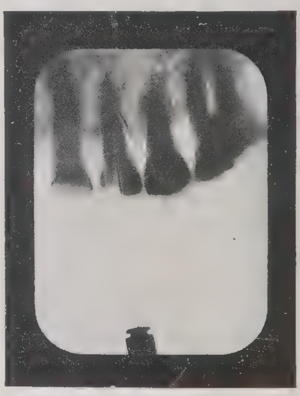


Figure 64. Putrescent bicuspid without apical involvement.

become focal on the entrance of bacteria. There can be no doubt that great damage has been done by this practice.

In Chapter 14 on Tooth Medications, I report our studies on the irritating effects of the medications currently used. Much work has been done since, demonstrating that dental medication may be a very definite cause of bone absorption about the apices of the treated teeth.

We very frequently see reports from non-dental diagnosticians, including roentgenographic interpretations of dental conditions, which specifically condemn and assign for extraction certain teeth which show evidence of apical absorption. Figure 59 shows a third molar with a zone of apparent decalcification which is in all probability an anatomically large medullary space, for this tooth is by all physical tests normal. Figure 60 shows lower bicuspids in which the mental foramen has been mistaken for an apical absorption. Figure 62 shows two centrals which have been condemned because of the apparent apical involvement but are due to the angle at which they are taken, throwing the root apex in such a relationship to the nasopalatine foramen, that it appears as an apical absorption. Figure 61 shows three illustrations of an anatomical relationship as it is disclosed by the roentgenogram, and which appears like an abscess on the palatal root of the upper molars, and is produced by the transparent zone of the maxillary sinus in alignment with the anteroposterior grooves.

Another type of irritation which can easily be misunderstood is that due to trauma, such as the overload in a tooth which frequently produces a very marked thickening of the peridental membrane, which, to the untrained, would readily be mistaken for a pericemental involvement. The removal of the overload, whether traumatic occlusion or the carrying of a fixed bridge, will usually entirely correct this condition. Another type of apical involvement also due to trauma of a different kind is produced in certain orthodontic procedures where, with the movement of the tooth, there is a distinct zone of rarefaction disclosed about it. Such a condition is shown in Figure 63.

It is, of course, understood that much of the data in this chapter should be common knowledge and is inserted here for the benefit of those not familair with these facts. The need for it has been suggested by a very large number of interpretations that have come to my hands, which indicated that the diagnosticians making them were not familiar with these facts.

It is common practice to depend upon the roentgenograms of teeth for a final decision as to whether they are or are not infected. I have previously stated that in our practice, approximately ten per cent of the teeth that we find to be infected and seriously injuring the patients, do not have the same revealed by the roentgenograms. Figure 64 shows a bicuspid tooth with a putrescent pulp, which condition is not suggested by changes in the supporting structures. In this patient's mouth several teeth were found similarly non-vital without any local symptom to suggest it. The patient was suffering from a nervous breakdown and her condition greatly improved following the removal of the non-vital teeth.

SUMMARY

We are led by these studies to conclude:

(1) **That dental infection will not of necessity produce bone absorption at the apex of the root of the involved tooth; and**

(2) **That absorptions, when they occur, are not of necessity a result of bacterial irritation.**

CHAPTER VII.

THE RELATION OF CARIES TO PULP INFECTIONS.

PROBLEM: What is the relation of the health of pulps without exposure to shallow and deep caries?

EXPERIMENTAL AND DISCUSSION.

Dental literature and dental practice have taken for granted that teeth, with exposed pulps as a result of dental caries, may be and probably are infected; but that teeth, with a dental caries which has not reached and uncovered a pulp chamber, are not yet infected, and are available and safe for filling by the indicated procedures. Clinical experience, however, has indicated to all observing operators that teeth with large fillings tend to develop symptoms, more or less severe, of pulp involvement, very often observed as hypersensitiveness to thermal change, and later pulpitis and pericementitis. So many teeth were found having non-vital pulps in which there were no symptoms whatever that the patient could distinguish that a series of careful studies was made to determine, if possible, the extent to which caries must have advanced before there was danger of pulp involvement, and what the early expressions in pulp tissue would be.

A practice, still more or less common but more generally practiced a few years ago, was that of pulp capping, by which some operators undertook to place over the zone of pulp involvement a non-irritating protection. Some of these were very ingeniously devised by making a little hood of gold or platinum into which was placed medicated paste, and the capping placed over the exposure and covered with cement, over which the permanent filling was placed. Statistics indicated that this operation was more likely to succeed in hot climates than in cold.

One of our experiences of years ago convinced us that there was danger in some of these pulp involvements to a degree far exceeding that which we had expected. A boy of fifteen years presented with a very acute rheumatism, being brought by a nurse from a Visiting Nurse Association. The history showed that four weeks previously he was compelled to leave school because of an acute tooth-ache definitely located in the left mandible. This acute pain lasted only a few hours; then it entirely disappeared. About a week or ten days later it was found that he could not get up from his seat in school and had to be carried home with acute rheumatism which kept him in bed for two weeks, after which he was hustled back to school. The teacher reported that he did not seem to care to play with the other children and seemed very tired, which she and the visiting nurse interpreted as being due to the lingering rheumatism. To our amazement we found a very bad endocarditis, with the heart greatly enlarged and already some cyanosis.

Examination of his mouth revealed deep caries without pulp exposure in the lower left first molar. The tooth was extracted and the boy ordered to bed under strict control of the district physician, which directions were not properly carried out; and he was buried in about seven months as a result of a complete breakdown of his heart. Before the tooth was extracted it was determined that the pulp responded nearly normally to irritation and thermal change. After extraction the tooth was sterilized externally, including the pulp cavity, and after the removal of the caries, culture was made from the pulp, which pulp, macroscopically, was nearly normal except that it showed slight congestion. Of thirty rabbits inoculated from this culture, 93.3 per cent, (28) developed acute endocarditis within a few days, and 100 per cent developed acute rheumatism. This, with many other experiences, made us very suspicious of the pulps of teeth with deep caries and prompted these special studies.

Teeth with more or less deep caries were accordingly selected for study. Figure 65 shows the pulp tissue underneath a caries that did not extend more than half way to the pulp but which was slightly abnormal to temperature change. The capillaries are enlarged and there is a marked infiltration of leucocytes just beneath the odontoblastic layer, with an area of necrosis. This patient had symptoms of an acute neuritis, which, incidentally, were greatly relieved by the extraction of the tooth; and it is very clear that a focal infection within the pulp is mechanically so situated that its toxic products must of necessity go into the lymphatic and hematogenous circulations; and, as necrosis proceeds, organisms can readily enter each of these two circulations.

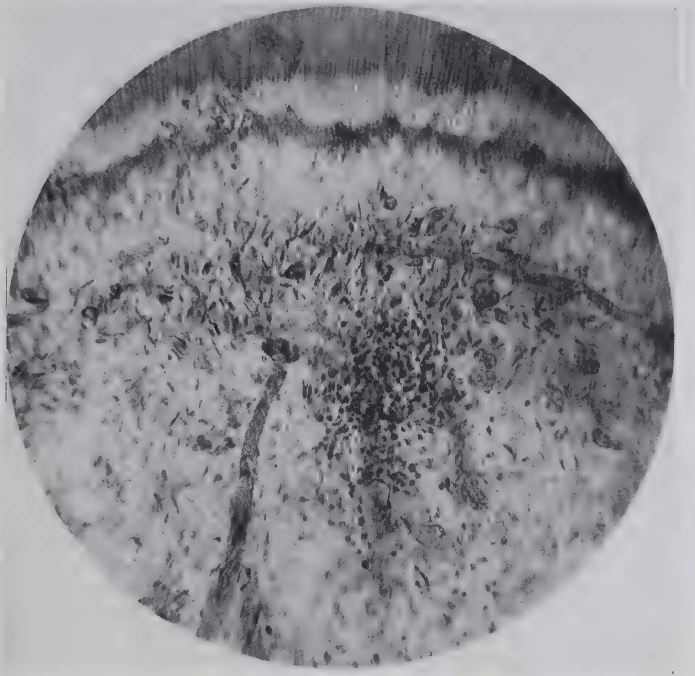


FIGURE 65 SHOWS THE PERIDENTAL LAYER OF THE PULP IMMEDIATELY BELOW A DENTAL CARIES. SEE FRONTISPIECE FOR HEMORRHAGE ASSOCIATED WITH PULPITIS.

In this case, as in many, the local symptom of pain and the reactions in the sympathetic nervous system were entirely out of proportion to the direct toxic reactions.

Figure 66 illustrates a very common type of pulp involvement following and accompanying deep caries. Figure 66-A shows a cross-section through the pulp of the three canals and the caries cavity on the mesial surface of an upper left second molar. It will be noted that the caries had extended only about half way to the pulp. Figure 66-B shows a roentgenogram of the tooth in the mouth with the metallic filling in place. In A is seen the location of a very large pulp stone, which type of calcification is expressing itself in many places as islands, as shown in Figure 66-D. There is a marked congestion of the blood vessels in the vicinity, which are shown in E. This was taken from the mouth of a man about sixty-five years of age, and his symptoms, as in the last case, were largely elsewhere; and it was only on testing that it was found that the pulp was abnormally sensitive to reactions from irritants. Figure 67 shows, similarly, extensive calcifications with multiple islands in a tooth with moderately deep caries but without pulp exposure.

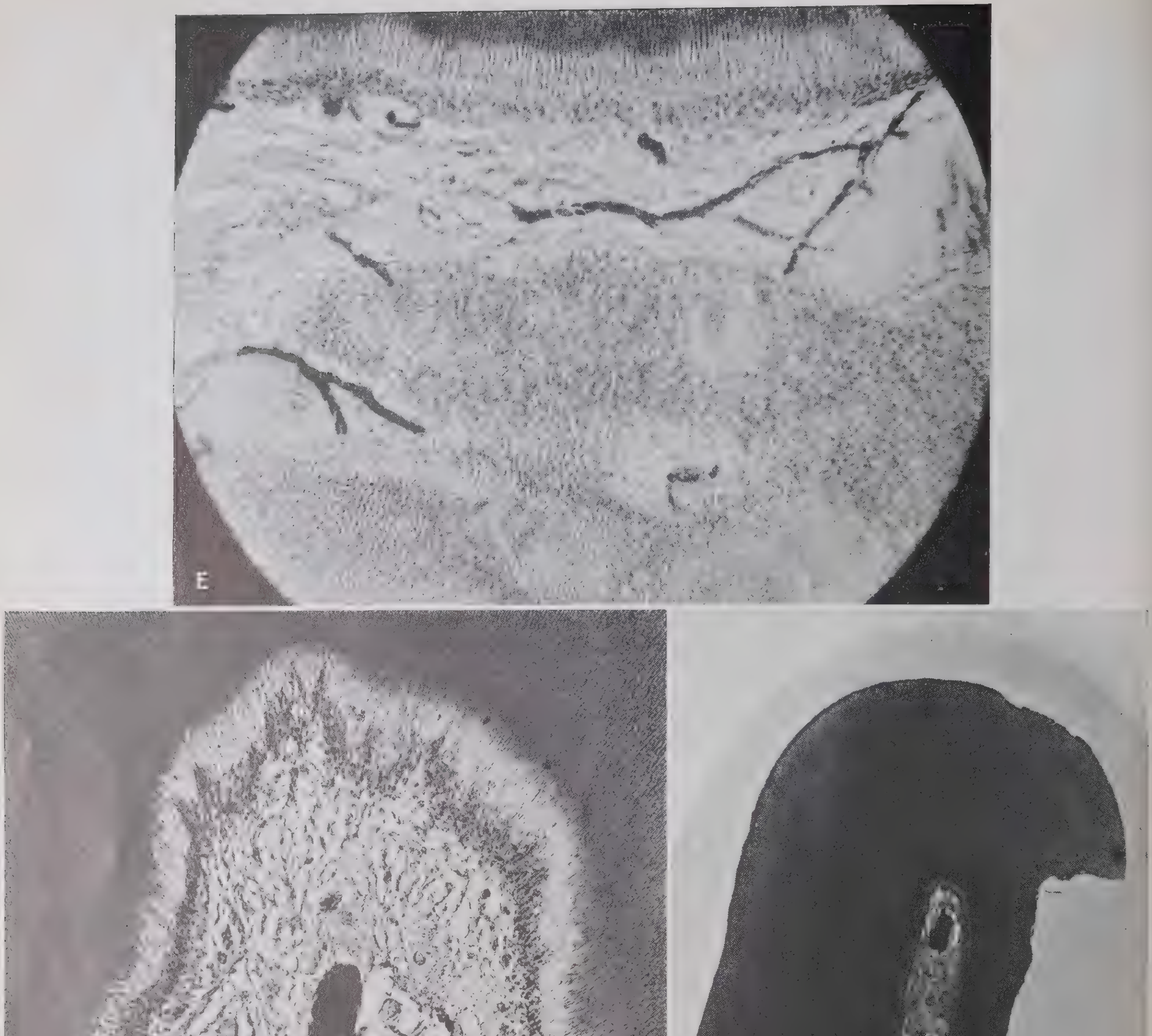


Figure 66. Pulp involvement and metallic filling: B, roentgenographic; A, cross section of cavity and pulp; D, pulp stones; and E, hyperemia and fibrosis.

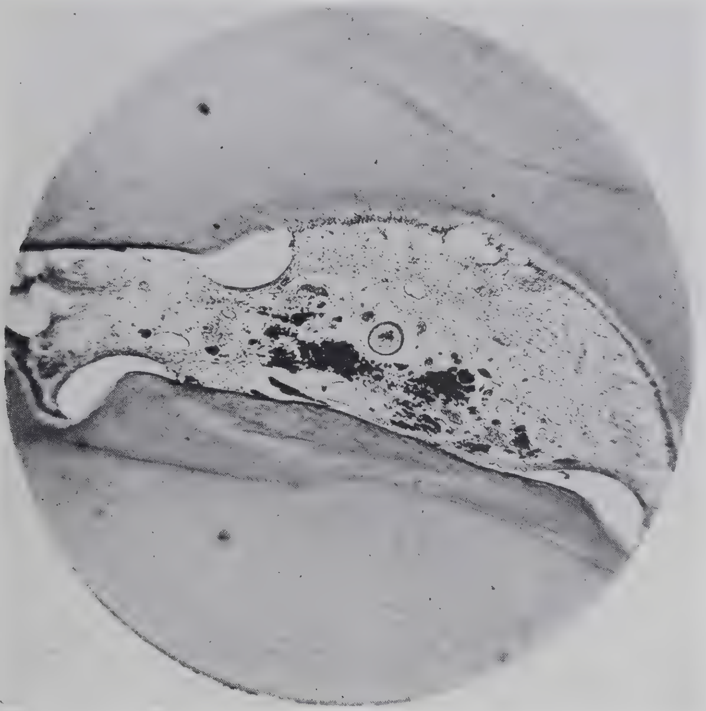


FIGURE 67. CALCIFICATIONS WITHIN PULP BENEATH MODERATE CARIES.

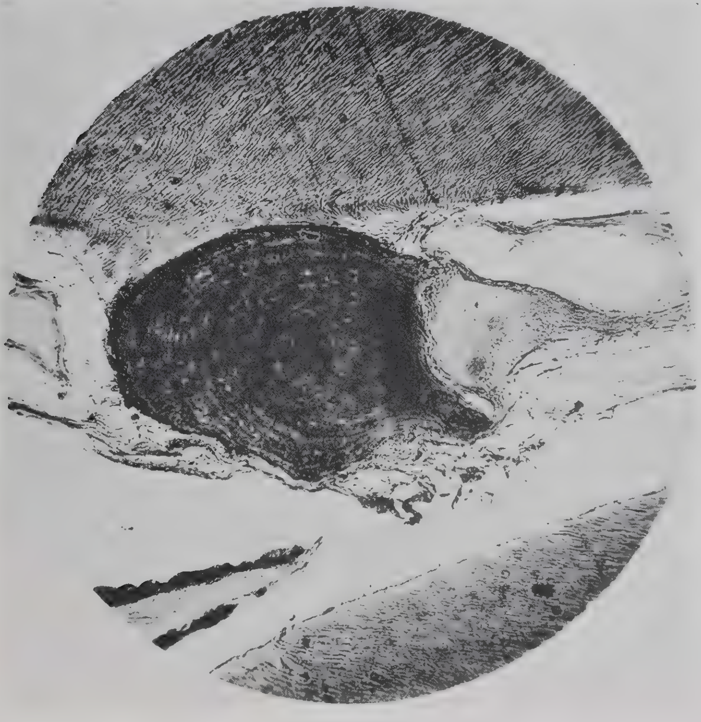


FIGURE 68. EXTENSIVE CALCIFICATION IN PULP OF TOOTH OF A BOY FOURTEEN.

It might be expected that a condition such as shown in Figure 66 might be found in the pulps of teeth of individuals of an advanced age, independent of irritation. We have, accordingly, made studies of the pulps of young individuals to determine whether the condition is independent of the sclerotic changes attendant with advancing years. Figure 68 shows a calcification in the pulp of a molar tooth of a boy about fourteen, the tooth having deep caries of long standing. It will be noted that the island is very large and shows distinctly a lamellar laminar structure, indicating that it was laid down in layers. It can readily be understood that, notwithstanding that this tooth had not yet given trouble, it would be very strange if it did not in the future.

A bacterial examination of the pulps of teeth with caries has revealed that in practically all cases of pulp culture of deep caries without pulp exposure, the pulps were found to be infected; and in teeth with moderate caries not extending more than one-fourth the distance to the pulp, the pulps were found infected in approximately 50 per cent of cases. It should not be implied that the presence of germs in the pulp would demonstrate that the pulp must later become a focus of infection, for it is definitely demonstrated that infections may involve the circulation temporarily as a result of acute colds and special epidemic infections.

This condition of calcification may be located in islands or be adherent to a wall of the pulp chamber, or may surround the pulp tissue on all sides and almost entirely obliterate it. Figure 69 shows two degrees of magnification of a section of the pulp through the root of a tooth where the calcification has reduced the lumen of the root to approximately one-eleventh of the original cross-section area. The dark area in the center is the pulp tissue; the granular layer is a calcified zone and is an osteoid structure. This tooth did not present local symptoms of abnormality, though the patient had very distressing symptoms of neuritis. Cultures from this tooth inoculated into animals developed very marked disturbances and pathological changes.

Some of these cases furnish the explanation for the so-called obscure neuralgias, the cause of which is ordinarily not found; and the patient may suffer both severely and long. Or it may be that the involved tooth may be located and proved to be one in which the dentist has placed a filling some months before; and the attitude of the patient will probably be one of very definite criticism of the judgment of the operator, assuming that he should

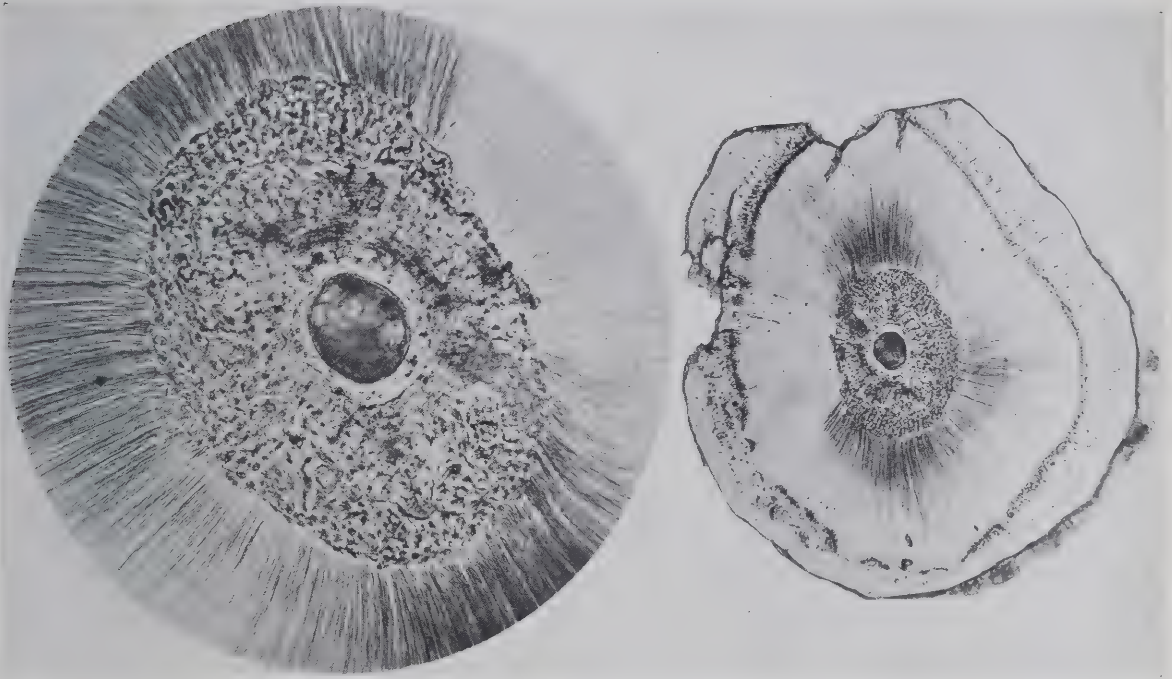


FIGURE 69. THE FILLING IN OF THE PULP CHAMBER WITH AN OSTEOID BONE.

have known whether or not it was safe to place an expensive gold inlay over the pulp of the tooth, even though, up-to-date, it had not given trouble. Unless the operator knows the probability of this type of pathology, he will find it very difficult to make a defense or explanation that will be satisfactory to the patient; and until the patients know of this danger they will continue entirely to misjudge the operator.

Figure No. 70 shows a case that illustrates this point. The patient has presented with an obscure neuralgia involving the left ear and the temple, with a symptom of hypersensitiveness to temperature change, which she locates in the upper teeth. No tooth is tender or has had a localized pain; yet the condition is severe. Careful examination reveals that the tooth that is abnormally sensitive to temperature change is the lower left second molar. An inlay placed three months before is in excellent condition. The history of the tooth is that the progressive caries had extended deeply, about half way through the dentin on both the occlusal and distal surfaces. On removal of the inlay, the dentin beneath a protecting layer of cement responded normally. It was decided that the pulp should be condemned and that this

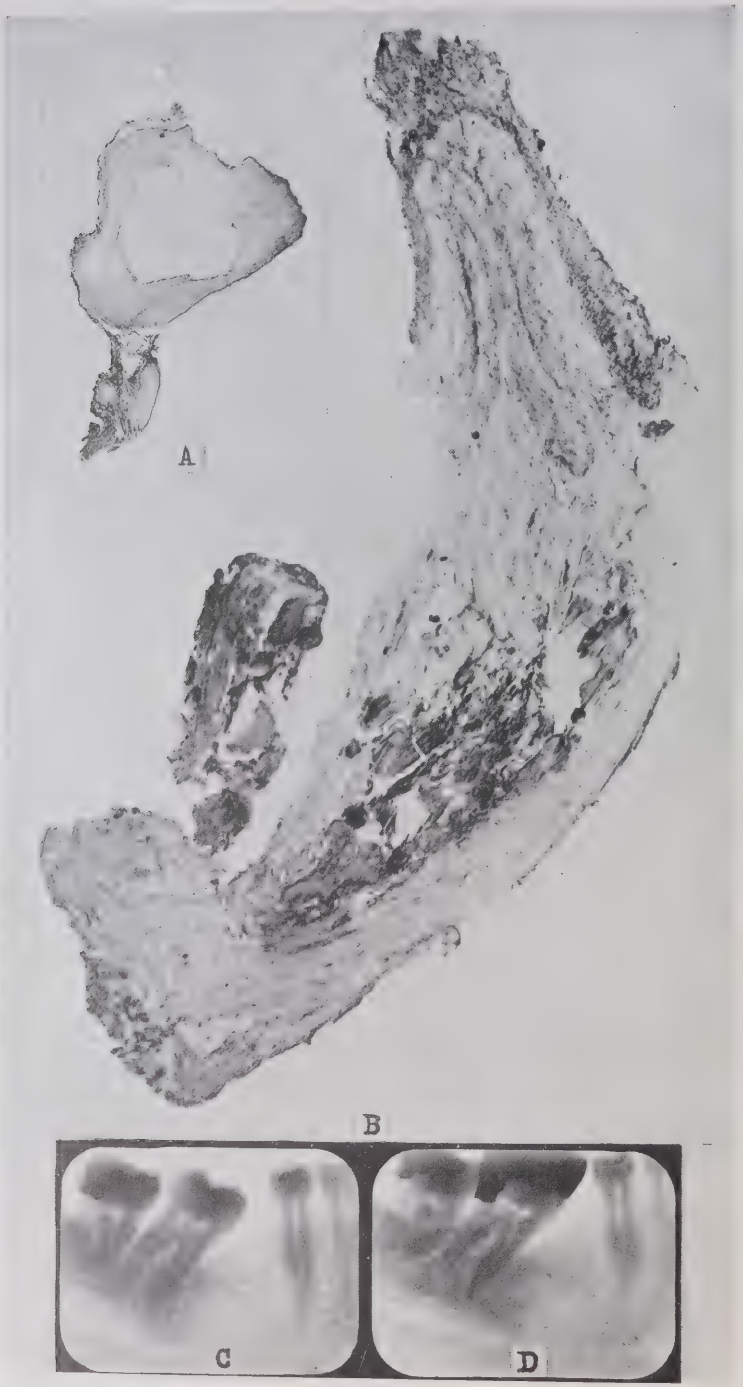


Figure 70. Pulp changes resulting from irritation of caries plus irritation of filling: C, original caries cavity in second molar; D, same with gold inlay; B, degeneration changes in pulp with fibrosis and calcification; and A, large pulp stone in coronal portion of pulp, not disclosed by Roentgen-ray.

patient could have the roots of this tooth filled, provided good access could be had. The pulp was removed under mandibular anaesthesia and sectioned. The pulp is shown in Figure 70 to have very extensive zones of calcification.

Other cases are shown in Chapter 66 on "The Nervous System and the Sense Organs."

Since the process of dental caries involves decalcification, the roentgenogram becomes a most important aid in detecting obscure zones and early stages of dental caries. This process of decalcification may be exhibited as extending from its beginning in the tooth to, or nearly to, the pulp. This is illustrated in Figure 71, in which a zone of decalcification is shown extending from a caries which has entered beneath an alloy filling and then has followed the dental tubuli directly toward the pulp. This is also shown clearly in Figure 72, in which the zone of decalcification can be traced in the roentgenogram from the open cavity directly toward the pulp. Figure B shows the pulp tissue directly beneath this zone of decalcification, and Figure C islands of calcification within this pulp tissue. The process by which the decalcification is carried on by bacteria and the systemic factors involved in it are discussed in Chapter 29 "Etiological Factors in Dental Caries."

I desire to present in this chapter an illustration of the progress of dental caries pulpward through the dentin. Figure 73 shows the details of the base of the cavity of dental caries in two magnifications revealing the etching of the tubuli and the advancement into these openings of the bacterial growth having entered the tubuli. The direction of this can most readily be made toward the pulp. The organisms furnish their own tools for dissolving the dentin, and progress as fast as they have enlarged the tubuli. B shows the enlargement of the tubuli far below the surface caries. The toxic substances produced by these organisms have as direct

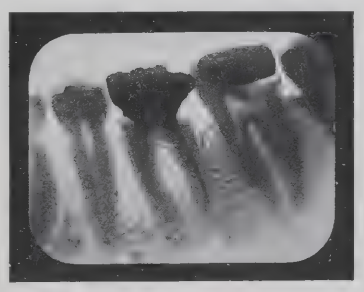


FIGURE 71. A ZONE OF DECALCIFICATION EXTENDING FROM THE CARIES CAVITY TOWARD THE PULP.
(See second molar)

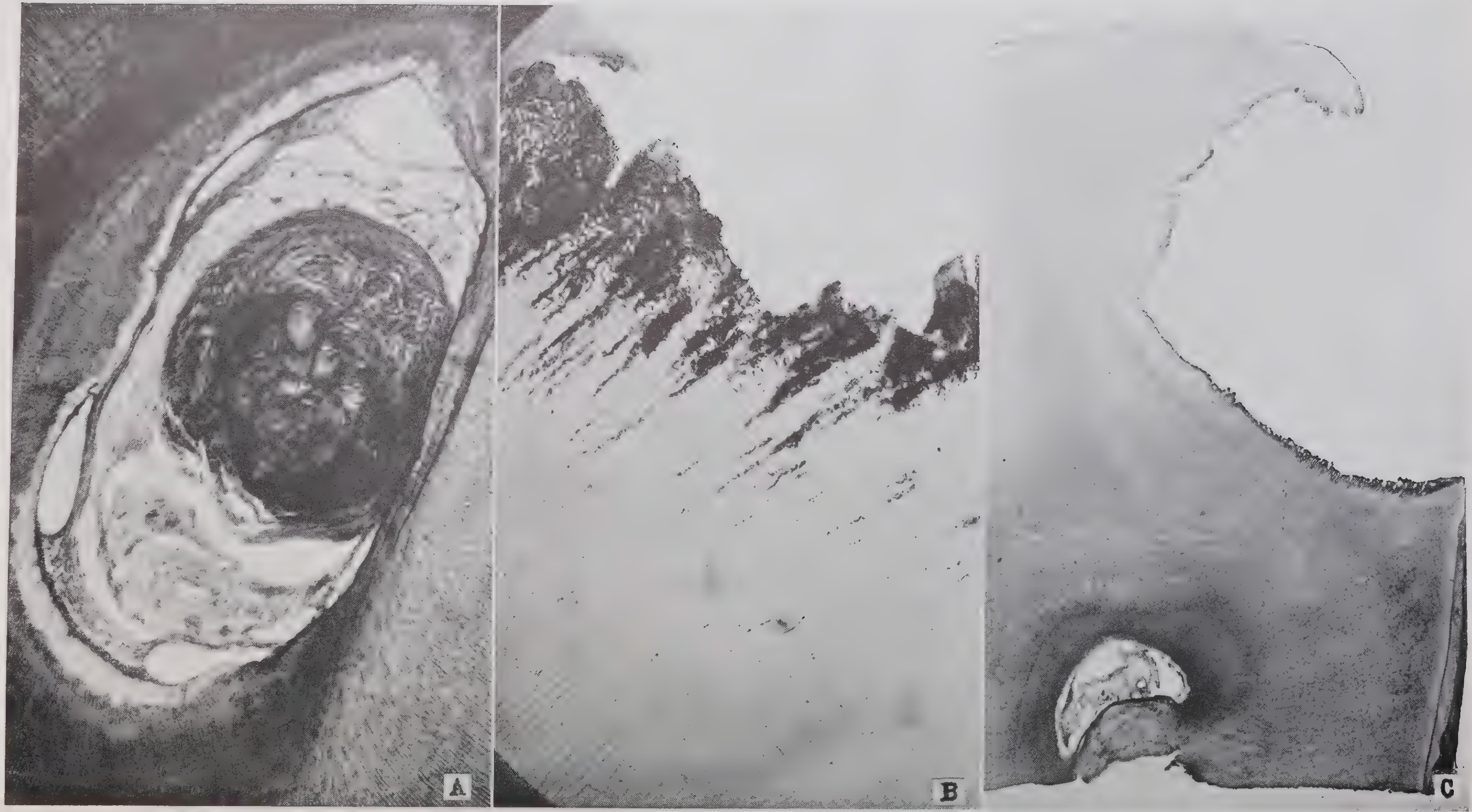


Figure 72. Sections of a tooth with deep caries, tracing changes to pulp: C, a cross section of tooth showing the relation of cavity to pulp; B. magnification of dentin showing advancement of decalcification following tubuli; A, a pulp nodule and fibrosis in pulp chamber.

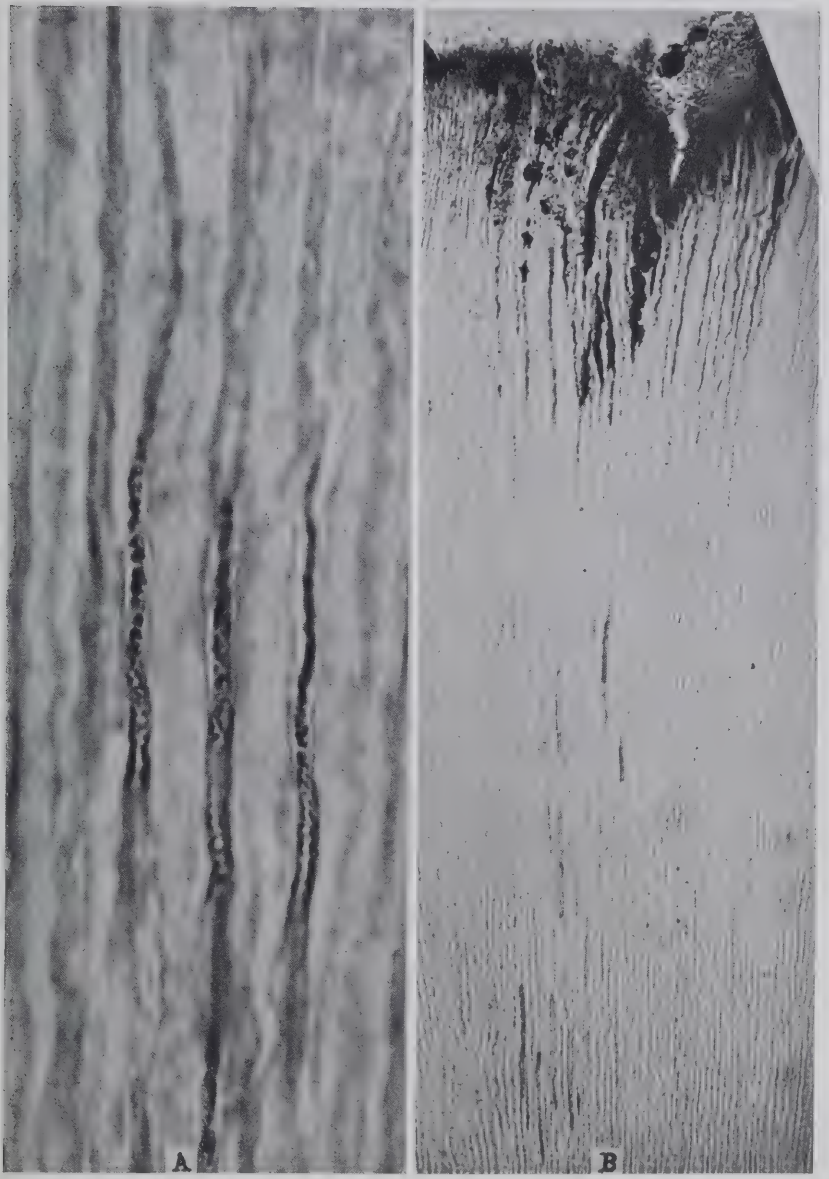


FIGURE 73. AN ILLUSTRATION OF THE DEPTH OF DECALCIFICATION FROM A SUPERFICIAL CARIES: B, FROM THE BASE OF THE CARIES CAVITY INWARD, SHOWING THE ENLARGED DENTAL TUBULI; A, ENLARGEMENT OF THE DENTAL TUBULI, SHOWING BACTERIAL ADVANCEMENT FAR TOWARD THE PULP.

access to the pulp as to the open cavity, and will most naturally develop in that direction, because it is in the direction of their food, since they live on the disintegrating tissue material which their own toxins devitalize in their advance.

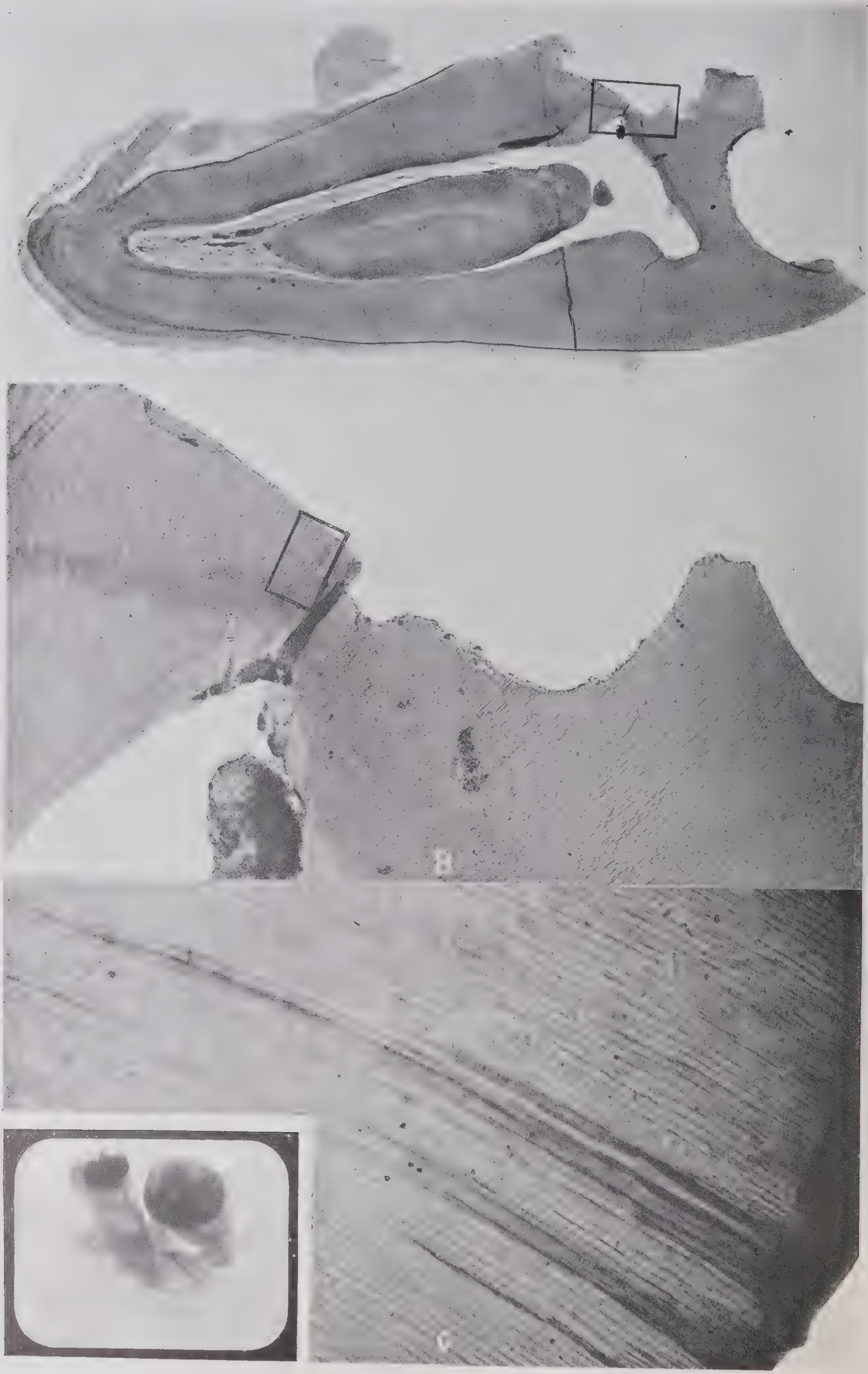


FIGURE 74 SHOWS PROGRESSIVE DEVELOPMENT OF INFECTION TOWARD THE PULP FROM CARIES CAVITY UNDER INCREASING ENLARGEMENTS IN A, B, AND C.

In Figure 74-A we have a cross section of the molar shown in the roentgenogram in 74-D. In the latter you will note a large alloy filling in the occlusal surface of the molar, and a distal cavity of caries at the point of contact with the malposed third molar. This tooth was vital and producing sympathetic disturbances from pulpitis. In B we have a magnification of the zone included in the oblong outlined in the margin of the caries cavity of A, but enlarged about 200 diameters; and in C we have a zone from the base of this area of the cavity, which is outlined in the oblong in B, enlarged to about 1200 diameters. In this latter the dentinal tubuli are shown enlarged to a point where the etching out of their lumina can be distinctly seen. The irritation upon the pulp tissue has been in progress for a long time, with the result that there has been a progressive degeneration, first as a congestion, then a fibrosis and calcification, the latter of which is shown in A at the point of fusion of the mesial and distal canals. This zone is shown enlarged in Figure 75-A; and it will be noted that in addition to the large islands that were so clearly seen and outlined in Figure 74-A, there are myriads of small ones resulting from the fibrosis. In Figure 75-B, a zone of the dentin beneath and at the margin of the leaking alloy filling is shown enlarged to about a thousand diameters; and in C, enlarged to about 1800 diameters. It would not be difficult to find arguments for and against the conclusion that the bodies shown are microörganisms. We will not introduce a discussion of this phase of the problem in this chapter. Whether these are organisms or products resulting from bacterial growth, the resultant irritation upon the pulp tissue has been very positive.

But these inflammatory irritations are not limited to the pulp itself, but are extended to the peridental membrane and the supporting structures. This is shown in Figure 76, A and B. In A we have marked changes in the vascularization. The large, dark, round area is a calcification within the lumen of a blood vessel. Between it and the cementum another blood vessel is shown in the process of degeneration. Transverse fibers are invaded with round cells and leucocytes, with much evidence of inflammatory process. These irritation processes produce at some points degeneration with absorption, and at others, prolif-

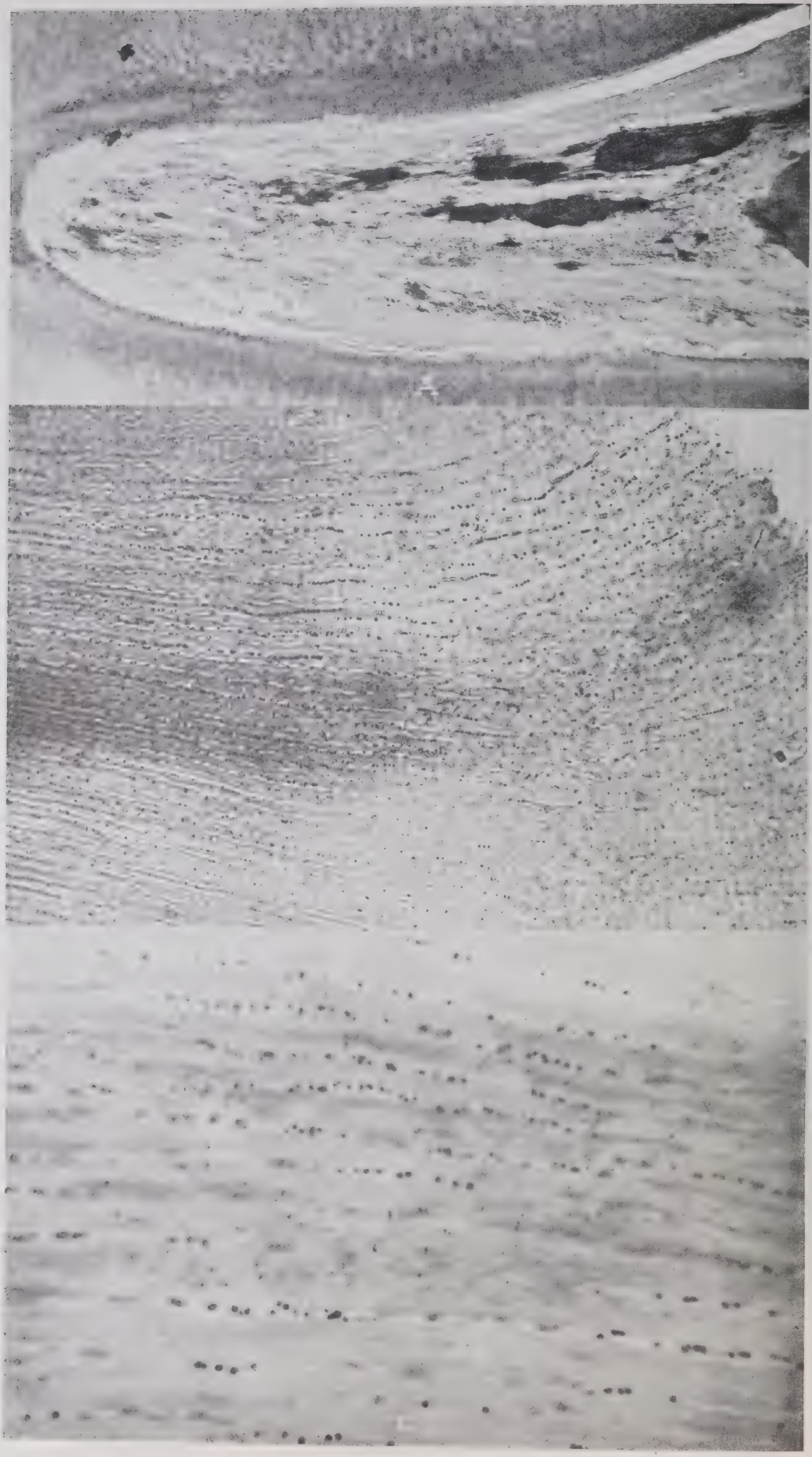


FIGURE 75 SHOWS CALCIFICATION ZONES IN PULP IN A; THE DENTIN BENEATH A LEAKING ALLOY FILLING IN B; HIGH POWER OF SAME IN C.

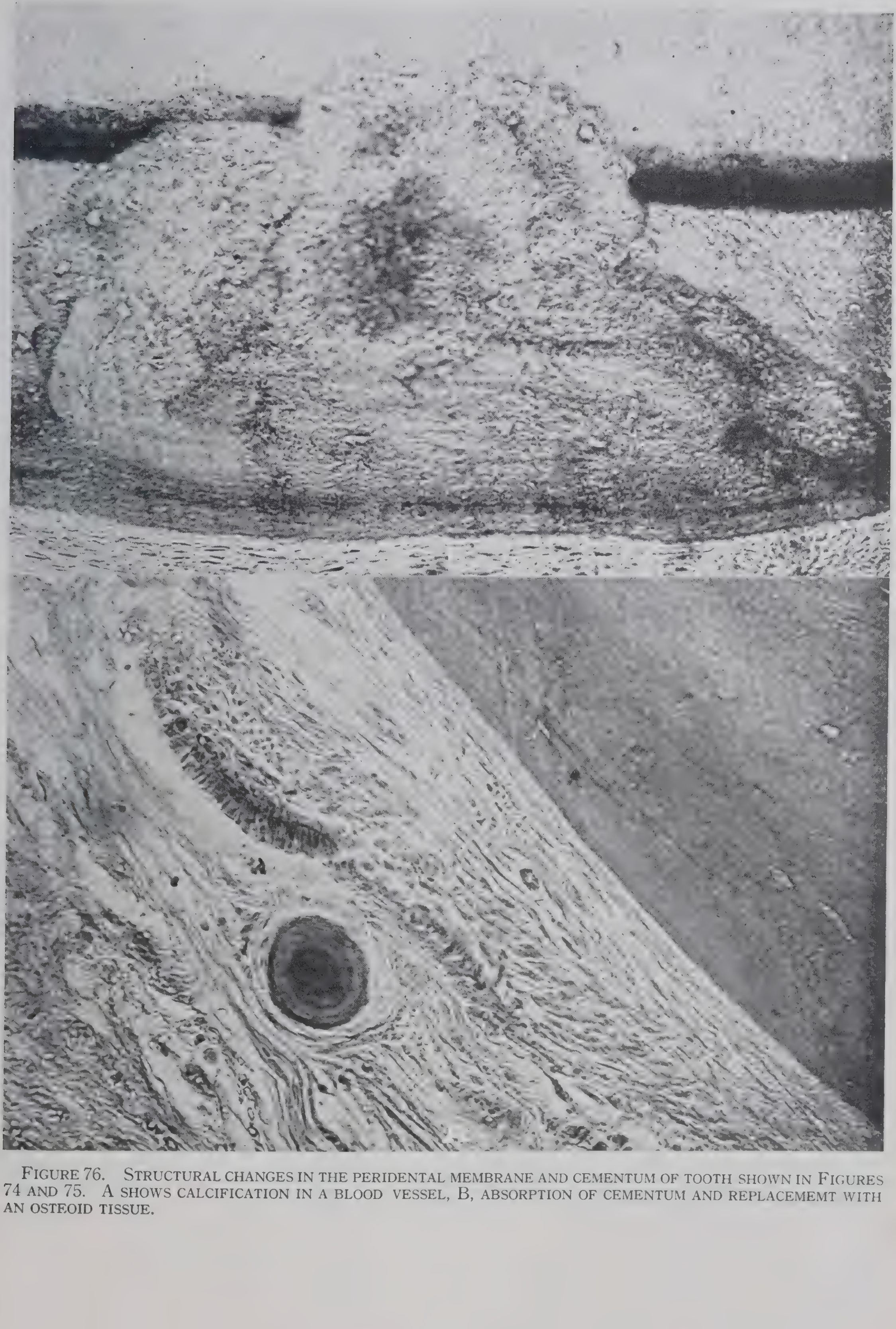


FIGURE 76. STRUCTURAL CHANGES IN THE PERIDENTAL MEMBRANE AND CEMENTUM OF TOOTH SHOWN IN FIGURES 74 AND 75. A SHOWS CALCIFICATION IN A BLOOD VESSEL, B, ABSORPTION OF CEMENTUM AND REPLACEMEMT WITH AN OSTEOID TISSUE.

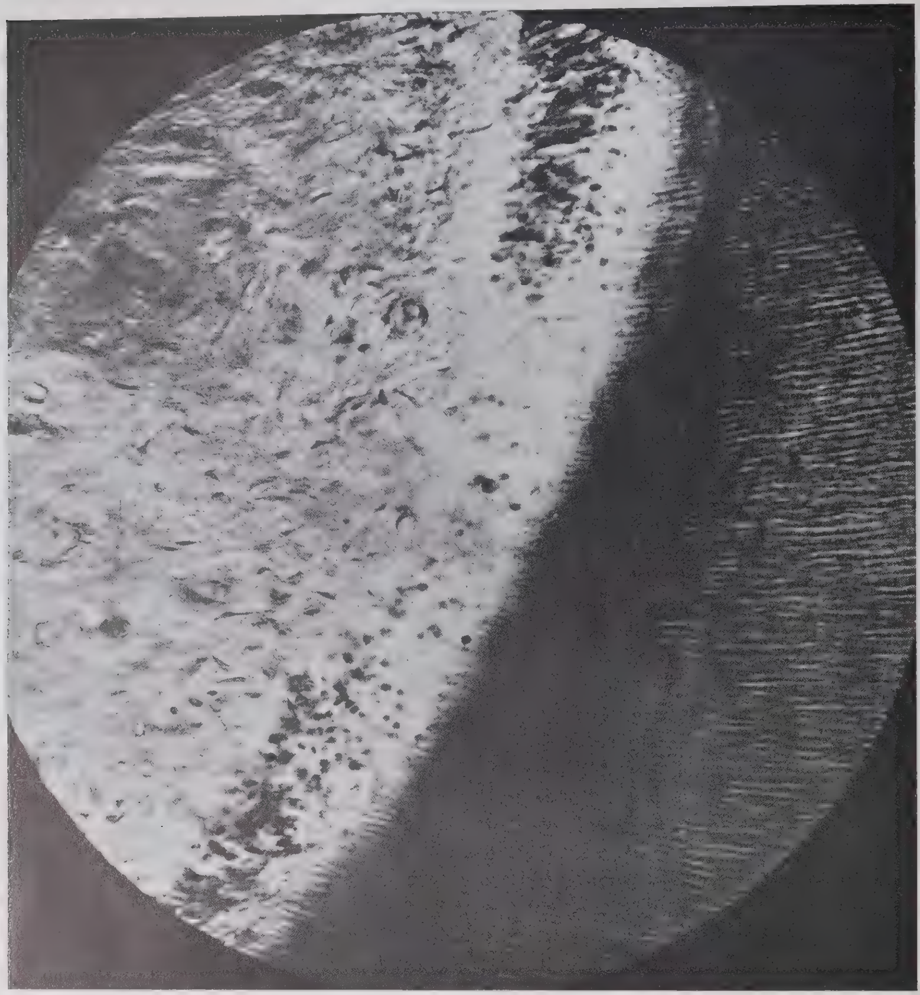


FIGURE 77 SHOWS A ZONE OF DEGENERATING OSTEOBLASTS BENEATH A ZONE OF CARIES.

eration with hyperplasia, as shown in B, in which an absorption cavity in the cementum has been later built in with osteoid structure; and these structures will always remain as scar tissues and with less than a normal defense against infection.

In Figure 77 we have a zone of the odontoblastic layer of the pulp just beneath a zone of caries. The toxic substances from the bacterial growth are penetrating into the pulp tissue. The odontoblasts in this zone have been devitalized. Their nuclei ceased to stain. Connective tissue is proliferating abundantly; and whether infection has already invaded the pulp or not, the scar tissue has been formed, which will probably express itself as a calcification and remain as a permanent injury to the function of the pulp.

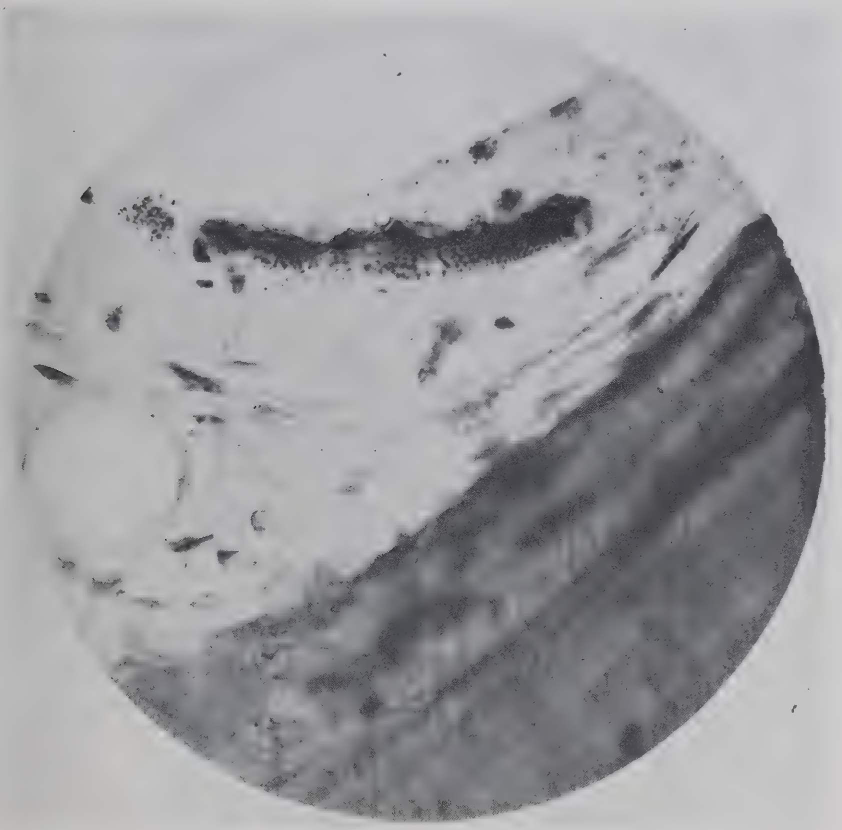


FIGURE 78. BACTERIAL INVASION AND NECROSIS IN DENTAL PULP BENEATH CARIES.

The bacterial invasion of the pulp usually progresses through the various stages of inflammation, first with congestion as part of the heroic reaction of the tissues to stamp out the invasion, then the paralyzing of the tissues and their degenerative forces with the resultant degeneration with the subsequent necrosis. At some stages of an acute pulpitis, bacterial invasion can be disclosed in the vital pulp. Such a case is shown in Figure 78, shown here stained with Giemsa stain. In this case there is marked degeneration of the odontoblastic layer, with fibrosis.

SUMMARY AND CONCLUSIONS.

This research has included the sectioning, culturing, and animal experimentation on many teeth with deep caries which were found to have abnormal reactions though nothing was disclosed by the roentgenograms; and has demonstrated to us that

> **Teeth with deep caries generally, and moderate caries frequently, already have their pulps involved from that source and cannot be dismissed as normal without further study by means other than the Roentgen-ray.**

CHAPTER VIII.

THE RELATION OF PERIODONTOCLASIA TO PULP INFECTIONS.

PROBLEM: Are the pulps of teeth influenced or injured by periodontoclasia (pyorrhea alveolaris) unless and until that pathological process has mechanically severed or invaded the vessels entering the tooth at the root apex?

EXPERIMENTAL AND DISCUSSION.

Dental practice and dental literature have recognized in the inflammations of the supporting structures of the teeth a direct danger of systemic involvement from the pathological processes about the tooth, but have taken for granted that the pulps are not in general involved except in very far advanced stages of this disease. These studies have accordingly been made to establish the earliest expressions of pulp involvement resulting from periodontal inflammation and infection. This particular chapter does not include the etiology of periodontoclasia. It has to do only with its effects on pulp tissue. Our interpretation of the etiology of this condition will be found in Chapter 28.

The earlier conceptions of this disease considered it as well nigh incurable, an opinion which does not generally obtain today. The newer conception regarding its amenability to treatment, however, has not recognized that even though the tissues about the tooth are put in relatively normal and safe condition, changes may have occurred in the pulp before that treatment was established, which may permanently jeopardize the pulp. Figure 79 illustrates such a case. In this case chronic periodontoclasia (pyorrhea alveolaris) had existed for years. The teeth were put under modern and efficient treatment; the disease was supposedly arrested; and the teeth became quite solid and comfortable. The old infection had, however, produced very extensive changes in the pulp tissues of these teeth. The pulp of this root had been divided by calcification which had extended across the entire pulp chamber. Very many pulp stones had formed. One is shown nearly half obliterating the remaining lumen. This tooth was still responsive to thermal change but was producing systemic disturbances. B, the insert, shows the roentgenogram of the tooth.

VIII-1

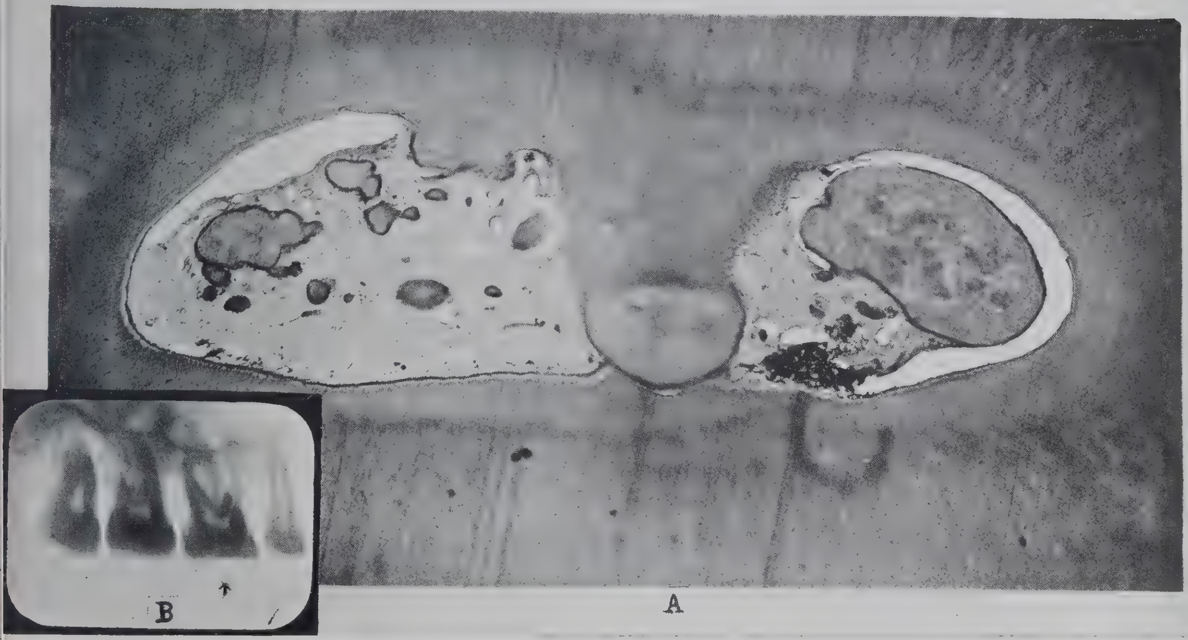


FIGURE 79. A DEGENERATING PULP, DUE TO PERIODONTOCLASIA. A, MULTIPLE PULP STONES, FIBROSIS; B, ROENTGENOGRAPHIC APPEARANCE.

The irritation from periodontoclasia may produce calcifications within the pulp chamber in a number of different forms. Whereas the tendency is quite largely to the formation of islands, it not infrequently occurs that a fibrositis develops within the pulp tissue, which later becomes calcified. We cannot conceive of a pulp's retaining its capacity for normal functioning, when such conditions develop, for it is embarrassed both by the osteoid structure within it which lowers the vitality of the pulp tissue, and by the abundant infection present in the vicinity which is available for infecting very quickly any pulp tissue in which the defense has become lowered. Such a case is shown in Figure 80. In this it will be seen that the pulp at the apex where it was subjected to the direct irritation of the toxic products is almost solidly calcified. Some nutrient vessels passing between these fibers maintain the vitality of the coronal portion of the pulp. These teeth have an entirely different relationship to the patient and his health in the early stages, when his defense is high and before the resistance of the pulp has been lowered, and it has been in-

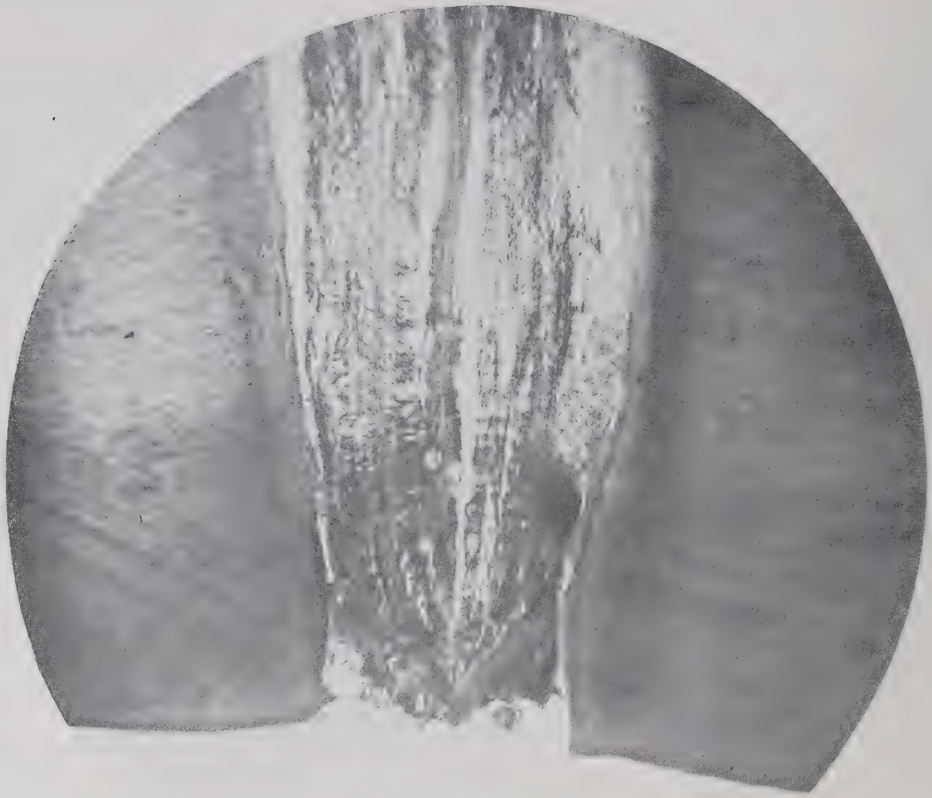


FIGURE 80. A FIBROSITIS OF THE PULP, FOLLOWED BY CALCIFICATION OF SAME.

volved, from the condition which exists in the patient with lowered defense and with this serious pulpal disease. From the patient's standpoint, and perhaps from most operators' standpoints, the tooth in the latter condition might be considered less serious because it is less loose than it had been previously. It may, however, have taken on a condition in which, with the patient's lowered defense, it may seriously jeopardize his health, or start a degenerative process in some organ or tissue of the body. This phase will, however, be discussed in later chapters.

I started investigations on this problem in 1916 while directing the activities of The Research Institute of the National Dental Association, which were carried out and reported by Dr. Katherine R. Collins,[2] which report was given before The National Dental Association in Chicago in 1917, and published in the

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[2] See bibliography.

Journal of the National Dental Association, VI, 1919, 164-170 (Information to Date on Infections within the Root and Periapical Tissues;) and pages 370-373 of the same journal (Preliminary Report on Bacteria Found in Apical Tissues and Pulps of Extracted Teeth).

Following this work some special studies were made by Drs. Hartzell[3] and Henrici,[3] University of Minnesota, and reported in the Research Jnl., 1, 1919, 419-422 (The Bacteriology of Vital Pulps).

SUMMARY AND CONCLUSIONS.

From these few selected illustrations of a general pathological reaction, it is evident to us that there may be a pulp irritation resulting from periodontoclasia long before a pocket has advanced to the vicinity of the apical third of the root. This irritation may express itself in very marked structural changes which may often be of a nature (because of calcifications), which will permanently destroy the normal functioning of the pulp. That such pulps can become the source of a focal infection involving the entire system has been abundantly demonstrated and is discussed in succeeding chapters, as is also the pathology of the changes which occur in pulp tissue, cemental tissue, and dentin. The evidence at hand suggests to us that

> **Deep pockets of periodontoclasia generally, and shallow pockets of periodontoclasia frequently, have already injured the pulp of the tooth, which tooth may be potentially much reduced in its safety from normal though it may have very great value and efficiency for mastication, and being potentially a danger must be continually watched.**

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[3] See bibliography.

CHAPTER IX.

THE RELATION OF DENTAL CARIES TO SYSTEMIC DISTURBANCE.

PROBLEM: Is there a relationship between susceptibility to dental caries and to systemic involvements of the rheumatic group lesions?

EXPERIMENTAL AND DISCUSSION.

We do not find in the literature or the fundamental thought of dental practice a clearly expressed conviction indicating the existence of a relationship between susceptibility to dental caries, and susceptibility to systemic involvements, and this study has been made to determine, if possible, whether there be any such relationship. We have carefully tabulated the presence of dental caries as a dominant factor in the life, or at some period during the life, of each of the cases here reported, inasmuch as that part of a tooth, that is once lost by decay, is always lost, for even though the tooth is filled, the mark of that ravage has been written in a form that cannot be obliterated. If the teeth are absent, true they may have been lost because of periodontoclasia. If, however, the teeth are present, showing very extensive fillings or open cavities, or absent, with no evidences of periodontal disease, it can be quite accurately determined that caries has been conspicuously dominant in the mouth being studied.

By dividing the patients into groups ranging from absence of systemic affection through mild to severe, and noting the proportion of dental caries in the mouths of these various groups, we are able to study relationships between these two types of disturbances. In Figure 81, we have in the first column the names of the groups in terms of their susceptibility to systemic involvement: namely, absent, acquired, inherited one side mild, inherited two sides mild, inherited one side strong, and inherited two sides strong; in Column two, the number of severe rheumatic group lesions in fifteen patients and their families; in Column three, the number of severe and mild rheumatic group lesions in fifteen patients and their families; and in Column four, the percentage of the group of fifteen individuals having extensive caries. From

Relation of *Caries* to Susceptibility to Rheumatic Group Lesions.
Fifteen Typical Families in each Group.

Susceptibility	No. of Lesions per Family		Per cent with Caries
	Severe	Severe and mild	
Absent	16	31	**40**
Acquired	63	96	**80**
Inherited 1 side mild	144	201	**67**
Inherited 1 side strong	258	338	**80**
Inherited 2 sides mild	227	308	**93**
Inherited 2 sides strong	483	754	**93**

FIGURE 81.

this chart it will be seen that in the first, the absent group, the percentage of individuals with caries, including mild and severe, is 40; in the second, the acquired group, 80; inherited one side mild, 67; inherited one side strong, 80; inherited two sides mild, 93; and inherited two sides strong, 93.

Even more striking is the parallelism between caries and the tendency to rheumatic group lesions, as shown in Columns two and three. In Column two, the total number of severe rheumatic group lesions found in the individuals and their families, with an absent susceptibility, is 16; acquired susceptibility, 63; inherited susceptibility, one side mild, 144; inherited, one side strong, 258; inherited, two sides mild, 227; inherited, two sides strong, 483. In Column three, the combined severe and mild rheumatic group lesions, respectively, are 31, 96, 201, 338, 308, and 754.

Relation of *Caries* to Susceptibility in 681 Individuals

Absent Susceptibility	Acquired Susceptibility	Inherited Susceptibility
73	130	327

FIGURE 82.

In Figure 82 we have divided all cases of caries into three fundamental groups of individuals: namely, absent, acquired, and inherited; and we find that in 681 individuals, 73 were classified as having absent susceptibility and caries, 130 acquired susceptibility and caries, and 327 inherited susceptibility and caries. The reader must distinguish that these are not ratios expressing caries in terms of susceptibility, but the number of individuals in the various groups who have caries. These studies show clearly that there is a very marked increase in susceptibility to caries with increased susceptibility to rheumatic group lesions whether or not either is causative to the other.

We have, accordingly, made an analysis of the different types of susceptibility for the purpose of determining whether or not caries bears a higher percentage of dominance in individuals with marked susceptibility to the various types of rheumatic group lesions. In Figure 83, we have related caries to each of the following: a susceptibility to digestive tract, internal organs, nerves, rheumatism, heart, and kidney; and it will be seen that these severe affections have been found in our groups to be associated with caries in ratios running from 70 to 100 as follows: Digestive tract, 70; Internal organs, 70; Nerves, 90; Rheumatism, 90; Heart, 100; Kidney, 100.

Relation of *Caries* to Type of Rheumatic Group Lesions

	Per cent
Digestive Tract	70
Internal Organs	70
Nerves	90
Rheumatism	90
Heart	100
Kidney	100

FIGURE 83.

RELATION OF CARIES TO SYSTEMIC SUSCEPTIBILITY

	Inheritance Group	No. of Families in Group	Percentage of Individuals with Extensive Caries
1	Dental Patients with *No* Developed Susceptibility	35	**51%**
2	Dental Patients with an Apparently *Acquired* Susceptibility	12 27	**91%** **78%**
3	Dental Patients with a Susceptibility and with one or both Parents acting as *Carriers Only*	16	**81%**
4	Dental Patients with a Susceptibility and with only *One Side of Ancestry*, including the Parent Involved	8	**88%**
5	Dental Patients with a Susceptibility and with *Both Sides of Ancestry*, including Both Parents Involved	7	**100%**

FIGURE 84.

In Figure 84, we have made a classification on the basis of susceptibility both where the parents acted as carriers only and where they were themselves involved from one or both sides of the ancestry, and have figures, as will be seen, ranging from 51 per cent in the absent group to 100 per cent in the inherited, both sides strong with both parents involved. This chart was made in 1919 and agrees in general with the recent findings of 1922, shown in Charts 81, 82, and 83. It shows dental patients with absent susceptibility, percentage of individuals with extensive caries, 51; acquired susceptibility, 91; another group of the same classification, 78; inherited susceptibility, one or both parents acting as carriers only, 81; inherited susceptibility, with one side of ancestry, including that parent involved, 88; with both sides of ancestry, including both parents, 100.

SUMMARY AND CONCLUSIONS.

From these data we feel compelled to conclude that one of these three conditions must prevail: First, that rheumatic group lesions are causative in the production of caries; or second, that dental caries is directly causative in the production of rheumatic group lesions; or third, that both are symptoms of a systemic condition. This will be discussed later.

We would accordingly change our previously accepted fundamental which concluded that there is no relationship between caries and systemic involvements to the following:

Susceptibilities to dental caries and to rheumatic group lesions are proportional, whether as cause and effect or as related symptoms.

CHAPTER X.

THE RELATION OF PERIODONTOCLASIA TO SYSTEMIC DISTURBANCE.

PROBLEM: Is there a relationship between susceptibility to periodontoclasia (pyorrhea alveolaris) and susceptibility to systemic involvements of the rheumatic group lesions; or stated differently, is it not true that with an increase of susceptibility to periodontoclasia there is a marked increase in sustibility to rheumatic group lesions?

EXPERIMENTAL AND DISCUSSION.

In undertaking the study of this problem, as herewith outlined, we seem to be wasting time with a fundamental that is so generally accepted that it must of necessity be correct. Surely with the increase in prejudice of various affections, from a relative indifference to dental decay and some apprehension for apical involvements and putrescent pulps, we come by progression, in the thought of the laity, and we think of the professions, in so-called periodontoclasia to the most dreaded of dental lesions. Many of the laity are as alarmed over the thought of periodontoclasia's having attacked their mouths, as they would be over some terrible affliction like leprosy. Such a firm conviction, it would seem, can only be born in fact. Probably few, if any, headlines in the advertisements of current literature will be so largely read as the advertisements for cures for periodontoclasia. We have, accordingly, taken up the study of this scourge with an expectation amounting to a confidence that our data will show conclusively that an increase in susceptibility and dominance of this affection will be continually accompanied by an increase in severity and susceptibility to the rheumatic group lesions.

In our careful analysis of these 681 cases, we have found 579 have had rheumatic group lesions, and only 102 were without rheumatic group lesions; and of the 681, 508 have extensive caries and only 155 periodontoclasia.

Relation of Periodontoclasia to Susceptibility to Rheumatic Group Lesions.
Fifteen typical families in each group. Group Two.

Susceptibility	No. of lesions per family		Per cent Caries	Per cent Periodontoclasia
	Severe	Severe and mild		
Absent	16	31	40	**40**
Acquired	63	96	80	**33**
Inherited 1 side mild	144	201	67	**33**
Inherited 2 sides mild	227	308	93	**20**
Inherited 1 side strong	258	338	80	**20**
Inherited 2 sides strong	483	754	93	**0**

FIGURE 85.

In Figure 85, we have related periodontoclasia to systemic involvements in association with dental caries as presented in Figure 81 of the previous chapter, No. 9. These data show in the last column, Group 1, that the percentage with periodontoclasia was 40, corresponding to the percentage with severe and mild caries; in Group 2, acquired, periodontoclasia 33%, caries 80%; Group 3, inherited one side mild, periodontoclasia 33%, caries 67%; Group 4, inherited two sides mild, periodontoclasia 20%, caries 93%; Group 5, inherited one side strong, periodontoclasia 20%, caries 80%; and in Group 6, inherited two sides strong, periodontoclasia 0%, and caries 93%; and in the entire 681 cases, periodontoclasia 23% and caries 75%. Columns three and four show respectively the total number of severe, and severe and mild lesions of the groups consisting of fifteen individuals and their families.

In Figure 86, in the chart made in 1919, Group 1, Patients with no developed susceptibility, severe periodontoclasia 23%, extensive caries 51%; Group 2, Acquired susceptibility, periodontoclasia 33%, dental caries 91%; Group 3, Inherited susceptibility with one or both parents acting as carriers only, periodontoclasia 25%, caries 81%; Group 4, Inherited susceptibility strong on one side of ancestry, including that parent, periodontoclasia 0, extensive caries 88%; Group 5, Inherited susceptibility with inheritance strong on both sides, including both parents, periodontoclasia 0, extensive caries 100%. By referring back to Figure 44, Chapter 4, the relationship of these figures to the increasing dominance of rheumatic group lesions will be readily seen.

Analysis of the 681 cases shows that in that number 167 had periodontoclasia, distributed in the three groups—absent, ac-

RELATION OF PERIODONTOCLASIA TO SYSTEMIC SUSCEPTIBILITY

Group One

Group	No. of Families in Group	Percentage of Individuals with: Extensive Caries	Percentage of Individuals with: Periodontoclasia
1 Dental Patients with *No* Developed Susceptibility	35	51%	**23%**
2 Dental Patients with an Apparently *Acquired* Susceptibility	*12 *27	91% 78%	**33%** **26%**
3 Dental Patients with a Susceptibility and with one or both Parents acting as *Carriers Only*	16	81%	**25%**
4 Dental Patients with a Susceptibility and with only *One Side of Ancestry*, including the Parent Involved	8	88%	**0**
5 Dental Patients with a Susceptibility and with *Both Sides of Ancestry*, including Both Parents Involved	7	100%	**0**

* Two groups.

FIGURE 86.

RELATION OF PERIODONTOCLASIA TO SYSTEMIC SUSCEPTIBILITY

	Susceptibility: Absent	Susceptibility: Acquired	Susceptibility: Inherited
Total No. of Patients	102	174	405
No. of Patients having Periodontoclasia	49	51	67
Percentage of Patients having Periodontoclasia	**48**	**29**	**16**

FIGURE 87.

quired, and inherited—in the following percentages: Absent susceptibility, 48%; acquired susceptibility, 29%; and inherited susceptibility 16%. (Figure 87.)

In Figure 88, we have made groupings in accordance with the type of lesion as we did in the previous chapter on caries. Digestive tract, periodontoclasia 20%, caries 70%; Internal organs, periodontoclasia 30%, caries 70%; Nerves, periodontoclasia 30%, caries 90%; Rheumatism, periodontoclasia 10%, caries 90%; Heart in patient and family, periodontoclasia 10%, caries 100%; Kidney, periodontoclasia 10%, caries 100%; Rheumatism and heart, periodontoclasia 0, caries 100%.

Relation of Periodontoclasia to Type of Rheumatic Group Lesions	% Caries	% Periodontoclasia
Digestive Tract	70	20
Internal Organs	70	30
Nerves	90	30
Rheumatism	90	10
Heart	100	10
Kidney	100	10

FIGURE 88.

In Figure 89, we have arranged a group of typical illustrations of gingival affections. In these, we have selected, as nearly as possible, the same irritant in the different classes of cases (and that a well known and all too common cause) namely, the impinging and irritating edge of bad fillings and open contacts producing food packs. In A, we see very extensive absorption of alveolar bone; in B, much less marked; in C, a slight area of absorption surrounded by an area of condensed bone; in D, practically no absorption of alveolar bone and a marked zone of condensed bone. When we relate these to susceptibility to the rheumatic group lesions, we find that A tends to be typical of those in the absent group; B and C, those in the acquired or mildly inherited groups; and D, those in the strongly inherited and strongly involved group. A survey of the illustrations that are used throughout the various studies, as in all the preceding chapters, will show how generally these conditions obtain.

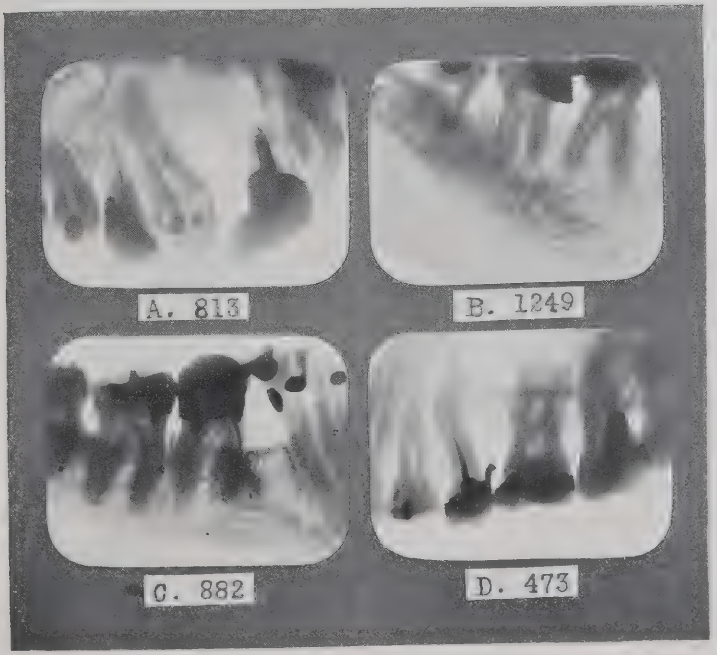

FIGURE 89. FOOD PACKS AND GINGIVAL IRRITANTS, WITH DIFFERENT TYPES OF REACTION.

In general, it is not true that, with an increase of susceptibility to periodontoclasia, there is an increase in susceptibility to the rheumatic group lesions; but on the contrary, those with no susceptibility to rheumatic group lesions, whether inherited or acquired, have a larger percentage of periodontoclasia (pyorrhea alveolaris) than any of the groups, ranging from mild to severe, of susceptibility to rheumatic group lesions. Our interpretation of these new and important phenomena will be given in the development of this general interpretation, in their places in subsequent chapters.

SUMMARY AND CONCLUSIONS.

From these data, we find an apparent contradiction to the thought and teaching of dental and medical science that is nothing short of bewildering. We have gone over our figures time after time to see if we have not made a mistake, but do not find such. Figure 86 made in 1919, and Figures 85 and 87 made recently, 1922, were made by different individuals. Those making the last charts not only did not know the figures of the previous study, but did not know that such a comparison had ever been worked out.

We are, apparently, dealing here with fundamental new truths which will have a great bearing on the explanation of the confusion which has been so dominant throughout the entire history of dental and medical science; and no conundrum has more completely and continually baffled solution than has the etiology of periodontoclasia, or so-called pyorrhea alveolaris. We would, accordingly, re-state the accepted fundamental, that with an increase of susceptibility to periodontoclasia, there is a marked increase in susceptibility to rheumatic group lesions to the following:

Individuals with marked susceptibility to periodontoclasia have, as a group, a decreased susceptibility to the rheumatic group lesions during the period of its active development (In its secondary stages it may contribute to rheumatic group lesions); or expressed otherwise, individuals with a very marked susceptibility to rheumatic group lesions tend, in general, to be free from extensive periodontoclasia; and when rheumatic susceptibility does develop, it would generally be classed as an acquired factor.

CHAPTER XI.

RELATIONSHIPS BETWEEN PERIODONTOCLASIA (PYORRHEA ALVEOLARIS) AND THE EXTENT OF PERIAPICAL ABSORPTIONS.

PROBLEM: Is there a relationship between the root end expression of irritation and the gingival expression of irritation; or otherwise expressed, is there in a given case no relationship between the size of apical abscesses from infected roots and extent of periodontoclasia?

EXPERIMENTAL AND DISCUSSION.

We do not find in the literature or the opinions of dental practice, evidence other than would tend to demonstrate or verify that there is no connection between the extent of the absorption, in case of apical abscess, and the extent and type of gingival absorption, as occurs in so-called pyorrhea alveolaris. These studies have been made to determine whether or not there be any such relationship.

In Figure 90, we have in the teeth of the upper arch (upper right first molar, upper left biscuspids and first molar) evidences of extensive periodontoclasia. The supporting alveolus has been very extensively destroyed, the gingival crest completely obliterated, and the lamina dura disintegrated to, or nearly to, the apices of the roots. In the lower arch will be seen a lower incisor and a cuspid root, each with periapical involvement, not of moderate degree but of great extent. This patient is fifty-two years of age, has never had any of the rheumatic group lesions, and not only has excellent health but carries an enormous overload of care and work all the time with apparent ease.

In Figure 91 we have a case with a marked tendency to periodontoclasia that has existed for many years but has passed from the active to the chronic stage. The patient is suffering at this time from an abscess in her scalp which she said seemed like a boil, though it has persisted in discharging for many weeks. She is fifty-seven years of age and has carried all this infection without injury until recently, when the above trouble developed, and also eye trouble. The upper left first bicuspid shows distinctly a

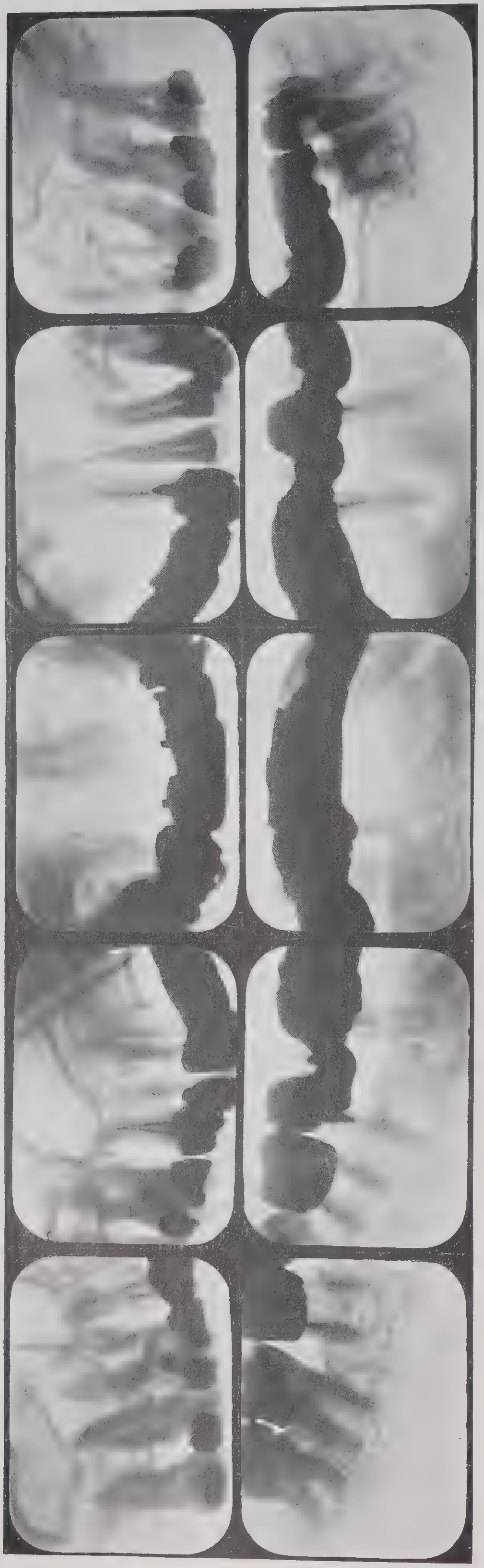

Figure 90. Extensive alveolar absorptions in both gingival and apical tissues, associated in the same individual.

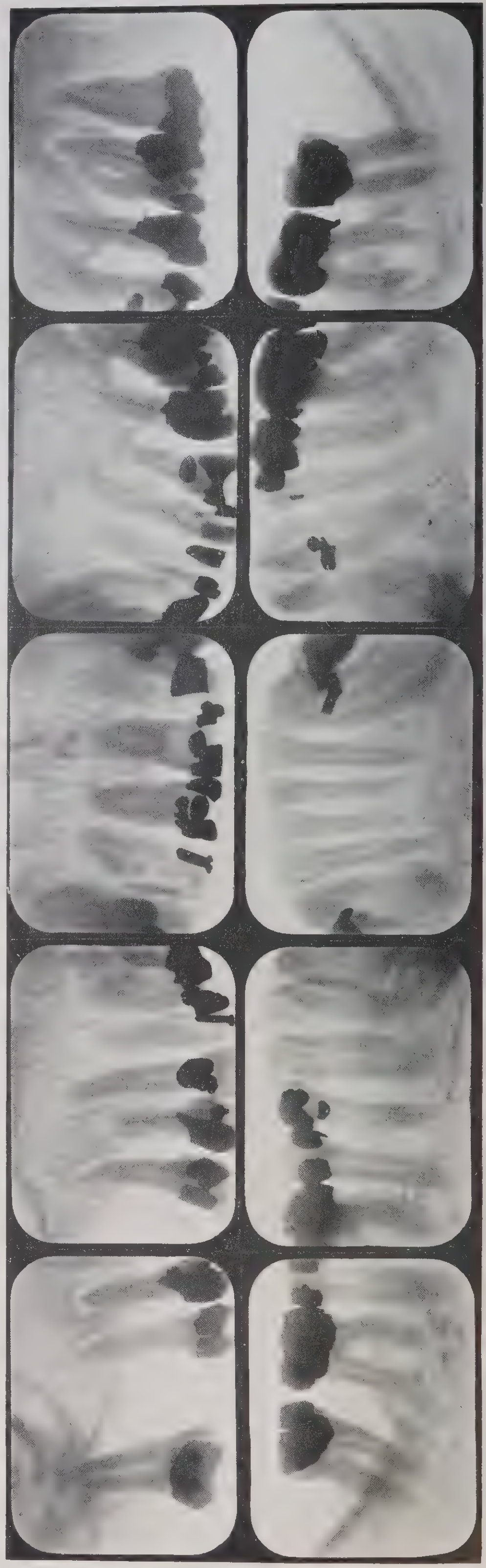

Figure 91. Long continued gingival and apical infection, with the resistance breaking.

zone of condensing osteitis about the rarefying from one view. This is also shown mildly about the extensive apical infections of the molars. This patient has reached the time when she can no longer defend herself against this infection. This patient has had, as will be seen, evidence of very extensive absorption about the molar roots. She has been entirely free from all rheumatic group lesions during her entire lifetime, until the beginning of the recent disturbances. These, incidentally, appeared simultaneously with a very severe overload occasioned by the illness and death of her sister, whose fatal illness had been caused by a septicemia resulting from a dental infection which had remained in a chronic condition for many years, but which, when her resistance went down at seventy-two years of age proved fatal after an illness of about six weeks.

In Figure 33, we have again much cause for irritation and practically no absorption of alveolar bone, no apparent tendency to periodontoclasia, and again pulp chambers with much cause for irritation and exceedingly little disturbance about the root ends.

When we relate these to the patient's susceptibility to rheumatic group lesions, we find in Case 1, practically no susceptibility and very marked periodontoclasia and extensive periapical absorption; in Case 2, mild periodontoclasia and apical absorption, and mild susceptibility to rheumatic group lesions, a condition frequently seen in acquired susceptibility; and in Case 3, no tendency to periodontoclasia and slight periapical absorption, and a strong tendency to rheumatic group lesions.

These three selected illustrations are not presented as being sufficient for final conclusions, but simply as typical illustrations; and an analysis of the illustrations of any of the chapters will show the same general principle. It must be kept in mind, however, that in order to make a comparison of reactions we must know that both the gingival and apical irritants were operating at the same period in the patient's life; otherwise, there may be an apparent contradiction, as, for example, if periodontoclasia were progressive during a period of high resistance, which for any cause was reduced so that the same irritations did not produce a continued progression of the absorption process, a condition of acquired susceptibility to rheumatic group lesions may develop, during which the defense is definitely lowered and consequently the reaction much less acute, in which state, caries may develop with pulp involvement, and with the characteristic apical reaction of an individual, without susceptibility to periodontoclasia, signifying simply a diminished or lost capacity for normal reaction.

SUMMARY AND CONCLUSIONS.

There is apparently a very definite relationship between these various affections and reactions, which we have discussed in later chapters; and we would, accordingly, restate the premise as follows:

> **There is a direct relationship between tendency to absorption of alveolar bone in response to irritation, whether at the gingival border or at the root apex; and individuals with extensive periodontoclasia have much more extensive areas of absorption at the apices of infected roots than do patients without a tendency to periodontoclasia.**

CHAPTER XII.

THE RELATION OF THE EXTENT OF ABSORPTION TO THE DANGER.

PROBLEM: Is the danger proportional to the evidence of absorption of bone about the apex of a suspected tooth?

EXPERIMENTAL AND DISCUSSION.

We perhaps should be expected to apologize for the presumption that there may be any question as to the truth of this so generally accepted premise. Probably in every city of any size in the country there are to be found would-be dental diagnosticians whose preparation presumably makes them competent to judge the difference in size of different areas with the naked eye, without a mathematical calculation, with considerable definiteness, but who have no qualification which would make it possible for them to interpret pathology in any other terms than dimensions. We must state frankly that this particular study was not inspired by any antagonism to these persons as a group, but solely in the interest of humanity. The fundamental basis for the procedure in the great majority of the laboratories of the country (and it is pathetically true that there is so great a majority of diagnostic institutions of the country undertaking to do dental diagnosis without the assistance of a trained dental pathologist) is to look in the roentgenogram for an area of radiolucency, and, if one be found, to judge its probable volume and extent, which factors alone determine whether that tooth is or is not potentially a possible source of danger to that patient; and in direct proportion to the volume will the danger be interpreted to be. We have, accordingly, classified fourteen hundred individuals in terms of their type and extent of absorption, both apparent and actual, in comparison with the presence and absence of systemic involvements.

In Chapter 5, when discussing the relationships between the characteristics of local structural change about infected teeth, and tendency to systemic involvement, I presented a series of cases as characteristic of the groups. While these did show those facts very strongly, and in accordance with the large number of cases involved in the various groups, they were not comparable

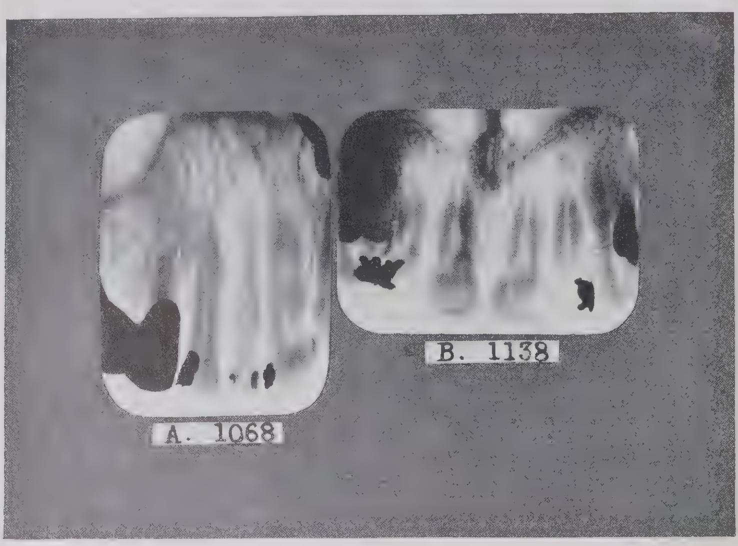

Figure 92. Laterals with putrescent pulps. Absent susceptibility.

infections in the sense that they were either the same type of infection or the same tooth. For example, areas of disturbance about root-filled teeth represent not only different sizes of teeth and numbers of roots, but a different capacity for infection within the tooth structure. Accordingly, if we can take a definite quantity of infection, such as would obtain with a lateral tooth with a non-vital pulp, and study it comparatively in different individuals, it becomes immediately possible to make comparisons with greater safety. In Figures 92, 93, 94, and 95, we have selected a series of infected laterals, which teeth had evidence of being non-vital for a considerable time.

Since the problem involved in this special research is to determine the relationship between the systemic involvement and the local expression, and whether the latter in its extent is directly proportional as a danger with that extent, it becomes immediately necessary that our study include a very careful analysis of the patients having, or not having systemic involvement, and of the same having evidence or proof of the dental focus as being a principal cause by the patient's being definitely relieved of severe symptoms by the removal of that dental focus.

When, now, we make a careful study of the systemic reactions and check them against these tissue expressions, we find that those in Figure 92 are free, and have always been free, from systemic involvements of the rheumatic group; in other words, belong to our group which we spoke of as absent susceptibility. Those in Figure 93, we find, have both been free during their lifetime until

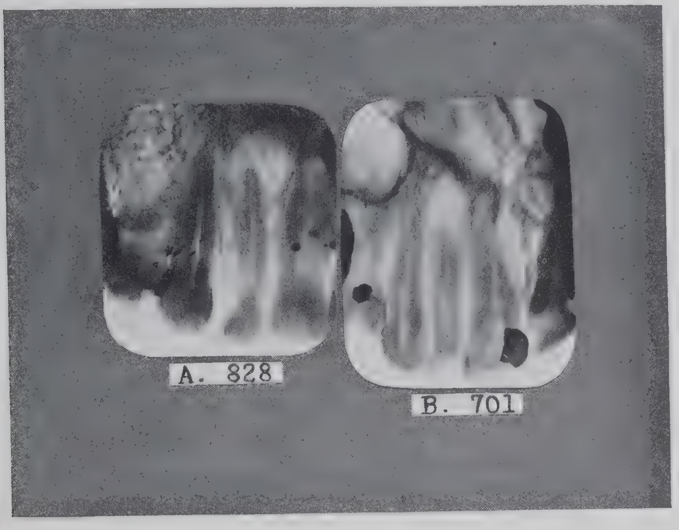

FIGURE 93. LATERALS WITH PUTRESCENT PULPS. ACQUIRED SUSCEPTIBILITY.

recently when they have had a sudden severe attack which has been entirely and permanently relieved by the removal of this dental focus. These patients belong to, and these illustrations are taken from, the group having an acquired susceptibility according to their systemic condition. Those in Figure 94, similarly belong to those with mildly inherited susceptibility; and those in Figure 95, with very little evidence of absorption about apices of infected teeth, all belong to the group which, according to their histories, have had serious involvements and have had a strong inherited susceptibility from both sides.

A clinical comparison of these individuals who represent different large groups reveals that those in Figure 92 have all the infection of a putrescent lateral pulp as have all the others, notwithstanding the fact, that they have never had any of the degenerative diseases which we speak of as rheumatic group. Fortunately these two individuals represent a large group of the total of society. During long periods of their lifetime their defense is ample to protect them against this and their various overloads and, as is so frequently seen, protects them against many such infected teeth. These two individuals are selected from the group of fifteen presented in Chapter 4, classed as those with absent susceptibility. The average number of severe rheumatic group lesions for the entire family represented by this group was found to be 1.07, and the severe and mild rheumatic group lesions 2.07. It will be remembered that, on an average, there are fifteen individuals included in the family circle of the ancestry.

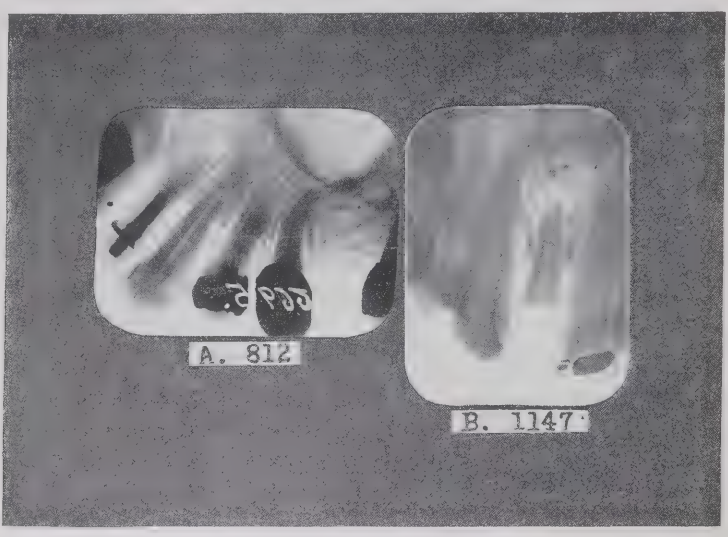

Figure 94. Laterals with putrescent pulps. Mildly inherited susceptibility.

The next two laterals, shown in Figure 93, are taken from the group with an acquired susceptibility. A is the lateral of a patient who has had a very unusually high defense all his lifetime until he was a victim of influenza. This lateral tooth had had a fistula for some time. With the onset of his Flu and following it, he suffered very severely from neuritis. This tooth was treated and root-filled and an apical curettement made, following which his neuritis promptly disappeared. Figure 93-B shows a different condition structurally in that there is a distinct tendency to the formation of limiting dense bone surrounding the rarefied area. This patient had been suffering for several weeks from rheumatism. This tooth was extracted and carried on a pinlay on the lingual surface of the cuspid. Her rheumatism seemed to be completely relieved by the removal of this tooth. These two individuals are typical representatives of the group which we have termed as having an acquired susceptibility. They, as a group, have had a high defense until an overload has broken them sufficiently so that they become a prey to their own infections, which previously they had carried without apparent injury. With the removal of their overloads or their dental infections, and particularly with the removal of both, they tend readily to come back to their own high normal. The individuals of this figure were selected from the group of fifteen, representing those with an acquired susceptibility, in which it was seen that the average total severe rheumatic group lesions of the entire immediate and ancestral relatives was 4.20, and the severe and mild 6.40.

Figure 94, A and B, shows two individuals with a mildly inherited susceptibility. They have tended more or less readily to have mild rheumatic group lesions with overload and infection. Whereas in the two former groups during the period of high defense, teeth tend readily to become tender and apical infections of this type nearly always have fistulae, in this group there is much less apical absorption for a given infection, less tendency to have a fistula, and less tendency to tenderness. With the removal of these dental infections which were of long standing, the results were as follows:

The patient represented in A, a married woman, age twenty-nine, had a severe nervousness following the death of her husband from influenza, from which she would cry on the slightest provocation, and had been incapacitated from her work, since she had to earn to support their four year old child. With the removal of her dental infections there was a rapid marked improvement in all of these nervous symptoms. She was able to take up her duties again and the world looked entirely different. However, just as grief is one of the greatest depressants and overloads, joys are among the most potential stimulants; and it is possible that one of the contributing factors to her vivacity and rapid return to health (although it is my belief that it came after this change in her physical condition) may have been the fact of a change in her life's responsibilities by a new engagement and a remarriage. Indeed, it is entirely probable that this happy change in her life could not have come for a long time, if at all, if it had not been by the remarkable change that was wrought by the removal of her dental infections. In these cases we have a combination of acquired factors superimposed upon the normal inherited tendencies. From her roentgenograms we would readily see that this woman's condition is indicated to be one of good reacting power and probably high defense. While this patient suffered from nervous breakdown, one of her sisters had a similar though less severe experience, and her mother and one of her mother's sisters had suffered very severely from nervous troubles. The health record, however, on the father's side was excellent, there having been no lesions of the rheumatic group recorded.

Figure 94-B is a case of a man forty-seven years of age, who has ordinarily had excellent health, but has recently suffered very severely from neuritis in his shoulders. With the removal of his dental infections, which were very extensive and of long standing, his neuritis entirely disappeared and has not returned, even in mild form for two years. This is a case where the factor of overloads was very important. This man had had very extensive dental infections. With the depression following the war, his business anxieties became very great. Rheumatism and neuritis had been mildly inherited from both his father and mother, and we should, accordingly, consider his case as being one of an acquired susceptibility superimposed upon a mildly inherited one. This is also indicated by the type of dental pathology revealed about his infected teeth, there being a zone of marked condensing osteitis surrounding the rarefying. The individuals of this group tend much more readily to have breaks from overloads than those in the two preceding. The susceptibility group to which they belong is mildly inherited, in which group of fifteen families we have found the average number of severe lesions per family group, inherited one side mild, to be 9.6, and the severe and mild, 13.4; and inherited two sides mild, 15.3 and 20.5.

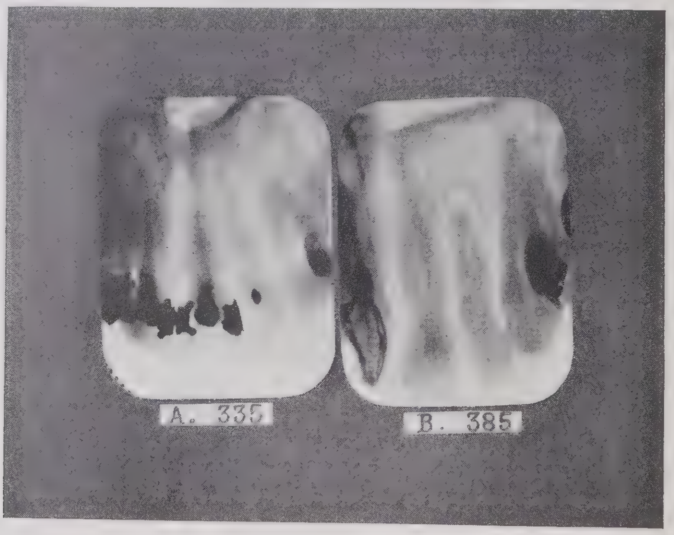

FIGURE 95. LATERALS WITH PUTRESCENT PULPS. STRONGLY INHERITED SUSCEPTIBILITY.

Figure 95, A and B, shows two cases from the strongly inherited susceptibility group of fifteen (in which group we have the average number of severe lesions per family group, inherited one side strong, to be 17.2, and the severe and mild, 22.5; and inherited two sides strong, 32.2 and 50.2) who are quite typical of that group. They are both young people. Each has a putrescent pulp in a lateral tooth. There is no fistula and never has been. The teeth are not sore and never have been, or but slightly. There is a very slight area of absorption about the apices of the roots. A has a type of nervous breakdown and rheumatism, and has been incapacitated from her work, or nearly so, approximately half the time for several years. This is only one of several dental infections that were removed, one at a time; and after complete removal of her dental infections, she has had very much better health and has scarcely lost a day from her work because of ill health for three years. B had a very severe heart involvement and rheumatism, which had completely incapacitated her from her work for several months. With the removal of this and other dental infections she very soon gained twenty pounds. Her heart is apparently normal in function again and her rheumatism entirely disappeared so that for several years she has not lost any time from this cause. A had previously had an operation for the removal of tonsils and appendix without beneficial result.

Each of these two individuals comes from a family with very marked susceptibility to the lesions from which they are suffering. Both of the parents of B died in the fifties of heart involvement after years of incapacity. A has some heart involvement. Her brother died of heart involvement as did her father, who also suffered severely from rheumatism. They are quite true to type for their class. The type of reaction about the apices of the roots shows progressively less destruction of alveolar tissue about the apices of the infected pulpless teeth; and with the decrease in apical absorption and the absence of fistulae, there is an increase in the susceptibility to systemic involvement, or a decrease in the patient's safety. This is precisely the opposite to what is taken for granted by the casual observations and as the general basis for the interpretation of dental roentgenograms.

And just at this point I wish to anticipate a misapprehension that is likely to occur. Individuals reading this must not quote this statement except in connection with the premises on which these observations are made and the comparisons given: namely, that with a given dental infection the apical reaction is progressively less with the decline of that individual's defense against that infection. In all these individuals, or more specifically stated, in any individual of any of these groups a larger quantity of infection will produce a greater local reaction of the type characteristic of that individual than a smaller quantity. Or otherwise stated, in any individual of any of these groups a tooth, with the quantity of infection so large as that involved with an entire infected pulp in addition to the infected dentin, will have a larger zone of disturbance about the apex of that tooth, than about some other tooth with a partial root-filling, and these two greater than some other tooth with an excellent root-filling, and all these three more than a tooth with a very recent suitable sterilization and root-filling. Accordingly, an individual with a very high defense and a very excellent reaction will show as much apical disturbance about a tooth with but slight infection, as an individual with a very low defense will about a tooth with a very large quantity of infection. We have, then, two important factors. A given amount of disturbance at a root apex will represent two entirely different quantities of infection with these different groups, and the danger to the individual having that given quantity of apical disturbance will be an entirely different matter, if she or he belong to the group having a very high defense, from that if they belong to a group with a very low defense, and these again will be directly related to their overloads.

We have made a careful study of the data disclosed in our records of case histories and find that in 681 selected cases having

RELATION OF LOCAL TO SYSTEMIC

Susceptibility Class	Local Expressions of Dental Infections						No. of Lesions per Group	
	Caries	Pyorrhea	Open	Locked	Rarefying	Condensing	Severe	Severe & Mild
Averages of Total No.	75	23	**25**	**75**	**32**	**26**	170	245
Groups of 15								
Absent	40	40	**40**	**60**	**67**	**0**	16	31
Acquired	80	33	**33**	**87**	**33**	**20**	63	96
Inherited 1 side mild	67	33	**40**	**87**	**33**	**20**	144	201
Inherited 2 sides mild	93	20	**27**	**80**	**40**	**33**	227	308
Inherited 1 side strong	80	20	**20**	**80**	**27**	**33**	258	338
Inherited 2 sides strong	93	0	**0**	**87**	**7**	**67**	483	754

FIGURE 96.

adequately complete histories, the average number of open dental infections, by which we mean infected pockets at the gingival margin of the teeth extending at least a third of the distance at the apex, or apical abscesses with fistulae, the average percentage of all types is 25, and the average percentage with apical infections without fistulae, termed locked infections, 75, the percentage with rarefying osteitis 32, and the percentage with condensing osteitis 26. (See Figure 96.)

When we select groups of fifteen from each of the six different degrees of susceptibility and compare the percentages for these four local conditions, we find for the absent group: open 40, locked 60, rarefying 67, condensing 0; the acquired susceptibility group: open 33, locked 87, rarefying 33, condensing 20; inherited susceptibility, one side mild: open 40, locked 87, rarefying 33, condensing 20; inherited susceptibility, two sides mild: open 27, locked 80, rarefying 40, condensing 33; inherited susceptibility, one side strong: open 20, locked 80, rarefying 27, condensing 33; inherited susceptibility, two sides strong: open 0, locked 87, rarefying 7, condensing 67.

From this it will be seen that there is a progressive change in the type of reaction directly in proportion as the susceptibility changes; the condensing osteitis progressing from 0 in the absent group to 67 per cent in the inherited two sides strong; and the rarefying osteitis decreasing from 67 per cent in the absent to 7 inherited two sides strong; and, similarly, the open decreases from 40 in the absent to 0 in the strongly inherited, and the locked increases from 60 in the absent to 87 per cent in the strongly inherited.

When we compare these figures with those in the next column—namely, the clinical expression of the rheumatic group lesions—called the Number of Lesions per Group, expressed as severe, and severe and mild, we have for the group with absent susceptibility as a total number of severe lesions in all or each one of fifteen individuals and all the members of their families—16, severe and mild—31; acquired susceptibility—63 and 96; inherited one side mild—144 and 201; inherited one side strong—258 and 338; inherited two sides mild—227 and 308; and inherited two sides strong—483 and 754.

SUMMARY AND CONCLUSIONS.

A study of the 681 selected cases from the 1400 here reported indicates to us that the danger is not in proportion to the area of apparent or actual absorption about root apices, and that it tends more nearly to be in a reverse order to the area of absorption produced by a given infection. Our interpretation of this is given in succeeding chapters.

This is a most important and striking discovery, and particularly so since the individuals recording these data and summarizing them had not the remotest conception of what was developing or its significance. It is a most singular fact that the presence of condensing osteitis in these groups should progress practically in direct proportion to the susceptibility to rheumatic group disturbances in the other members of the family as well as in direct proportion to the susceptibility in the individual. The former is a fact of profound significance. It is a very different thing that the type of local dental pathology should be related to these qualities in the other members of his or her family. We are therefore dealing with common effects of general causes.

We would therefore state the fundamental on which this research is based as follows:

> **Since different people react differently through a wide range to a given infection, the quantity of the absorption is not a measure of the danger but, on the contrary, it may be, and frequently is, true that the patient suffering severely from a systemic reaction caused by a dental infection, shows very little absorption compared with that which the same dental infection would produce in a patient with ample and high resistance.**

CHAPTER XIII

THE NATURE OF THE DISCHARGE FROM A DENTAL FISTULA.

PROBLEM: Is the discharge from a chronic dental fistula badly infected and very poisonous?

EXPERIMENTAL AND DISCUSSION.

Pus has been synonymous in the thinking and teaching of dental problems with concentrated virulent infective organisms, so much so that until recently it has been thought that teeth with fistulae draining apical abscesses were not only the most dangerous but, until the advent of the Roentgen-ray, constituted nearly the entire group of so-called abscessed teeth, and therefore the cure of the pathological lesion in question depended entirely upon the skill of the operator. The proof that the abscess was cured was the closing of the fistula.

Years of experience in oral surgery revealed that practically all of the teeth that were removed as border-line, proved to be seriously involved at the apex, though without a fistula. For years it was deemed that teeth were not bad enough to be border-line if they did not have a fistula; but if they were not bad enough to have a fistula, it was taken for granted that they were all right, that they were of necessity not badly infected; and those with fistulae were presumed by many operators to be incurable or not, depending solely upon the skill of the operator, and particularly on the magic secret formula which he possessed, most of which teeth required many and long treatments according to the ideals of those days. This phase of the problem, namely medication, is discussed in the next chapter. It is possible that even today it is well nigh universally believed by the members of both the medical and dental professions, and for that matter the laity also,that teeth with flowing fistulae have the same only because they are more severely and extensively infected than the teeth that do not have fistulae. In other words, the presence or absence of a fistula is a measure of infection.

This problem has to do with the nature of the material flowing from chronic dental fistulae. The method of procedure has been

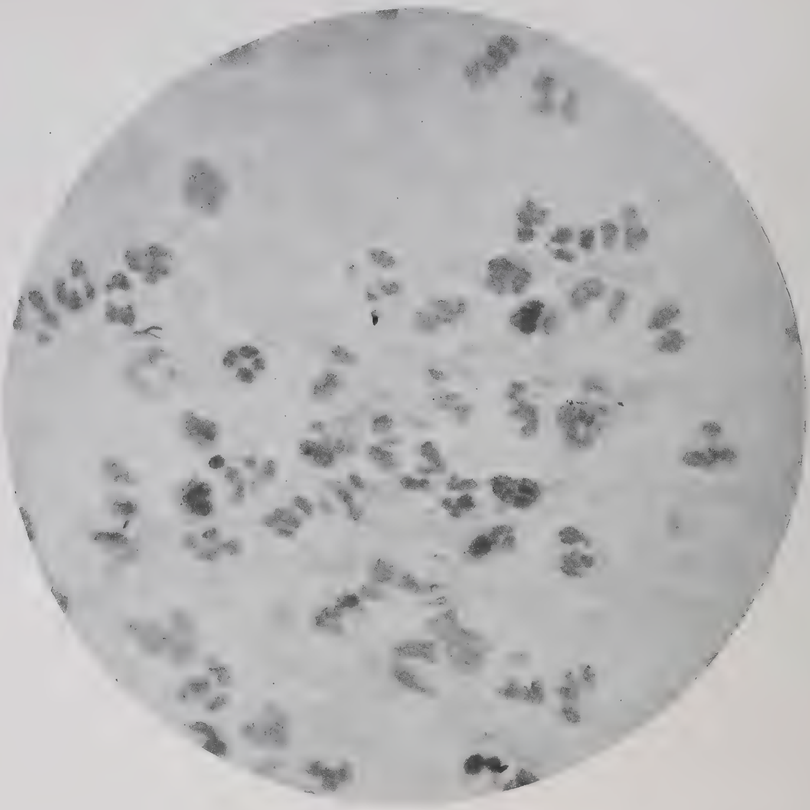

FIGURE 97. DISCHARGE FROM A FISTULA OF A PATIENT WHO HAS A HIGH DEFENSE.

to take by aspiration, material from the fistulae and study its contents both in living and stained mounts. Since this material is supposed to be made up, in addition to the leucocytes, with living and dead organisms, stains were expected to show large numbers of organisms free in the fluid. Figure 97 is typical, being a Wright's stain, and it will be noted that while there are many polynuclear leucocytes, only a small portion of them contain phagocyted organisms, and there are practically no organisms outside the leucocytes. Many phagocyting leucocytes have only 1 or 2, a few have 5 to 10, but the great majority do not have any. Plating of aspirated contents from agar media frequently reveals only scattered colonies, and not infrequently aspirated material from dental fistulae, cultured in suitable media, proves sterile.

Let us now study the patient from whom the pus was taken from this flowing fistula. The roentgenograms of the teeth are shown in Figure 98. She is forty-six years of age, with a very unusual physique, in that she has never had any of the rheumatic group lesions, nor have any of the members of her family. She has several poorly filled root canals, which if they had been in the mouth of an individual with low defense and marked rheumatic group susceptibility, would have had very little apical disturbance and no fistula. But in her case practically every imperfectly root-filled tooth shows extensive apical alveolar absorption. She has fistulae both in the hard palate and through the buccal mucous membrane, has frequent swelling, will feel very miserable for a day or two while fighting the acute attack, and with its subsidence rebounds quickly to her normal high defense and excellent health. She is relatively safe so long as she has this undisturbed high defense; and since her normal by inheritance is so high, only a severe overload will break it. Any of the severe overloads which we discuss later, such as influenza and pregnancy, would tend to make her splendid defense less complete and her factor of safety would be definitely reduced, perhaps to the danger line. This type of individual should live to be ninety or one hundred, with good health to the end. She may develop nephritis, hypertension, or other degenerative diseases as her defense goes down with advancing years; and since the chain is no stronger than its weakest link, her efficient and healthful life term may be reduced a decade or two or three by the presence of these very dental infections, for she will go into the class with an acquired susceptibility.

We will later discuss, but will anticipate here, the type of individual furnishing most favorable conditions for the various operations such as root-filling, apicoectomy, etc. It will, however, be readily seen that if such operations are to be made, they will be much more favorable of success in the individuals with the high defense, as we have outlined it, than those with the relatively low defense. In other words, such an individual as we have shown here, could doubtless have root fillings made in these roots, and root resections, and be relatively safe in carrying these teeth for a few years because of her normally high defense, not only because of the operation that might be made but, in fact, in spite of any dental operation that might be made. We will later discuss in further detail the many overloads that may come suddenly and make the individual suddenly susceptible to the infections to which he has previously been relatively immune.

This quality of the nature of the discharge from a fistula varies greatly with the stage of the break or absence of break in the defense. We have very frequently seen, and this can be observed

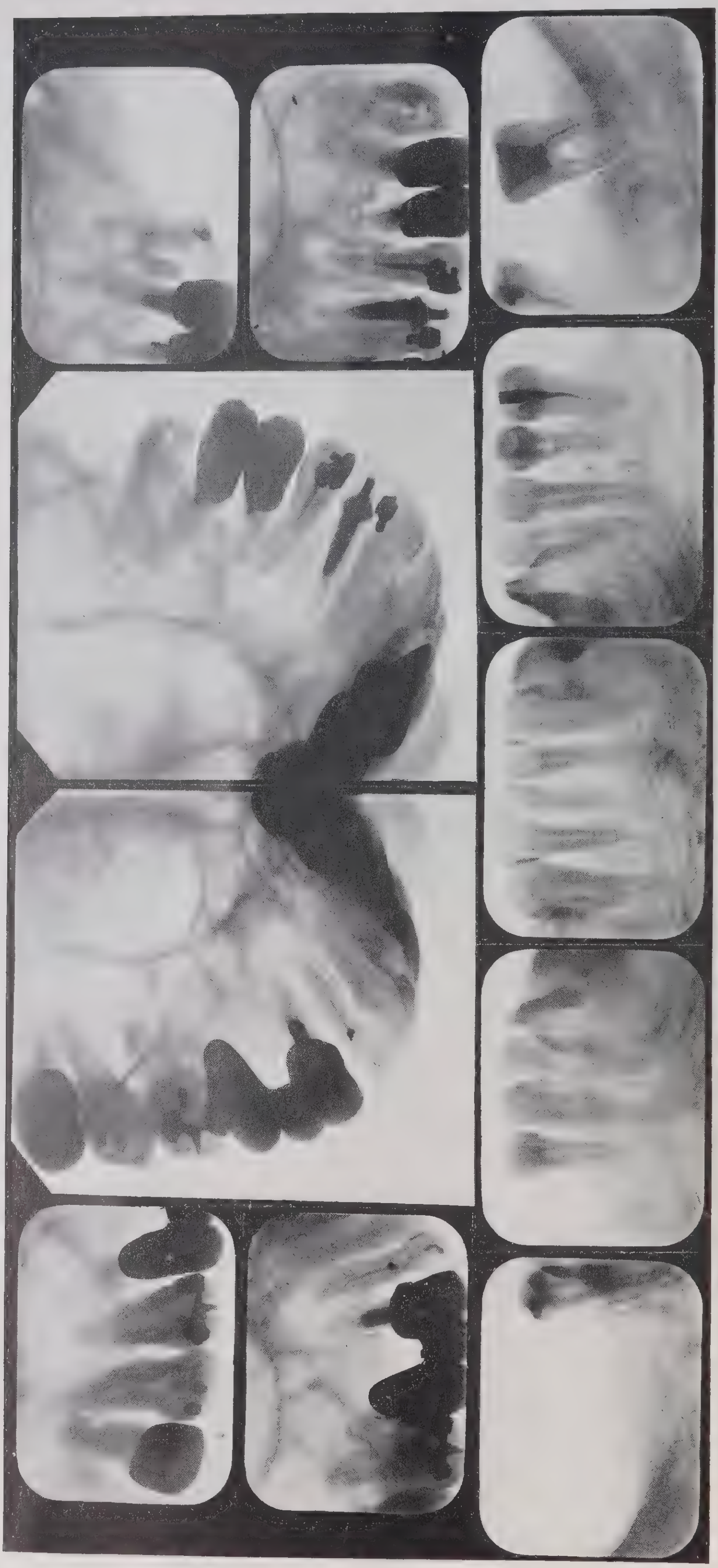

Figure 98. Appearance of periapical reaction of patient who has a high defense, referred to in Figure 97.

in many mouths, the scar of a fistula which has closed, not because the conditions have become better though they apparently have, since the flow has stopped, but because the conditions have become worse. Very many fistulae close, following an attack of influenza. In subsequent chapters I will discuss some qualities of the mechanisms involved. Incidentally, it has been because of the finding in the clinics, particularly the outpatient clinics of hospitals, of large numbers of individuals with flowing pus from fistulae about broken down and carious roots and no rheumatic group lesions, the patient having come because of a specific infection or traumatic injury, that large numbers of the medical and dental profession have concluded that if people with so much dental infection as these individuals apparently had, do not have rheumatic group lesions, then dental infections are not capable of producing so serious disturbance as some of us have claimed. In other words, these expressions of defense have been mistaken for evidences of quantity of infection. I would ask the reader to look again carefully at the root fillings in the teeth showing these large apical areas in Figure 98, and compare the quantity of infection possible in these teeth with the quantity available with an entire putrescent pulp, as shown in the various individuals in Figures 92, 93, 94, and 95, in the preceding chapter.

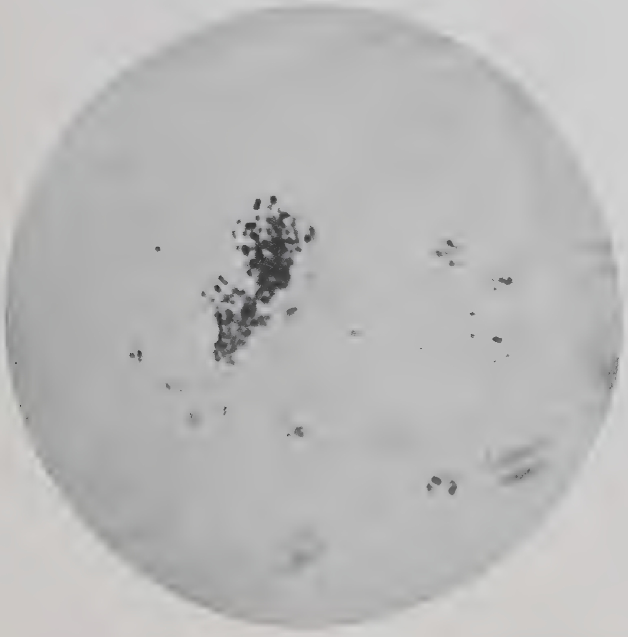

FIGURE 99. SMEAR FROM ROOT APEX OF TOOTH OF FLOWING FISTULA. ONLY PHAGOCYTED ORGANISMS ARE SEEN.

A smear from the apex of a root of a tooth with a flowing fistula

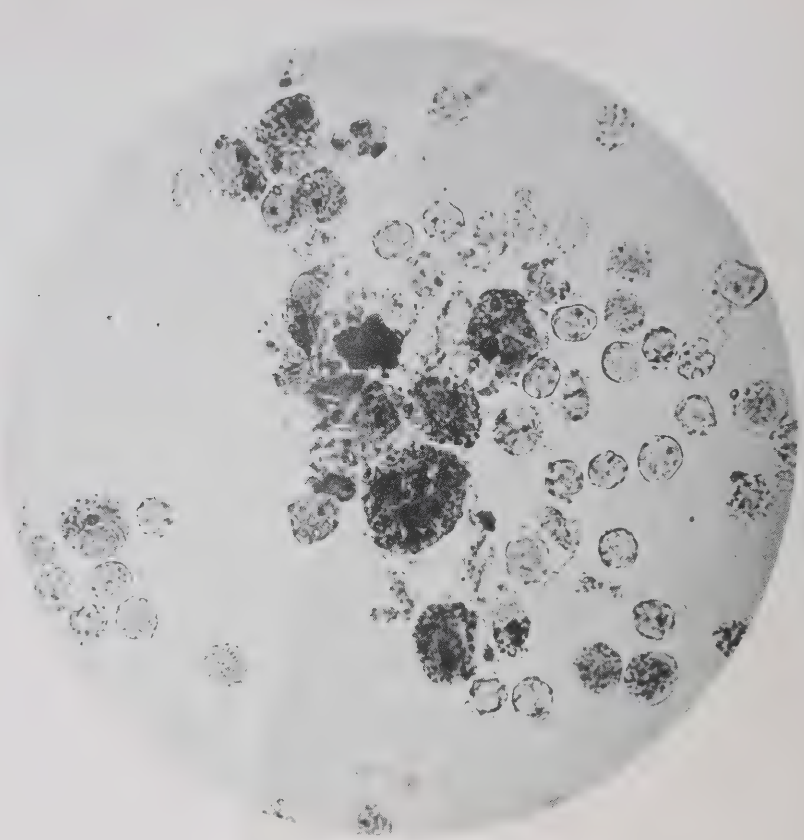

FIGURE 100. A PROFUSE PHAGOCYTOSIS FROM A FLOWING FISTULA.

shows practically no organisms except those few that are phagocyted. (See Figure 99.) In this instance the smear does not show a large number of leucocytes. Some other cases do show a very profuse infiltration of leucocytes with a large proportion of them phagocyting leucocytes. This is illustrated in Figure 100. Figure 101 shows a smear from the root of a tooth without a dental fistula, and while it is not necessarily typical of all the various types of apical involvement without fistulae, it is typical of a very large number; and in it, it will be seen that there are large numbers of organisms free in the fluid and not yet phagocyted, beside those contained in the phagocyting leucocytes. This would appear to be quite the reverse condition to what is generally expected to obtain, though we will see in the discussion of this phenomenon that it is what we should really have expected if our interpretations are correct.

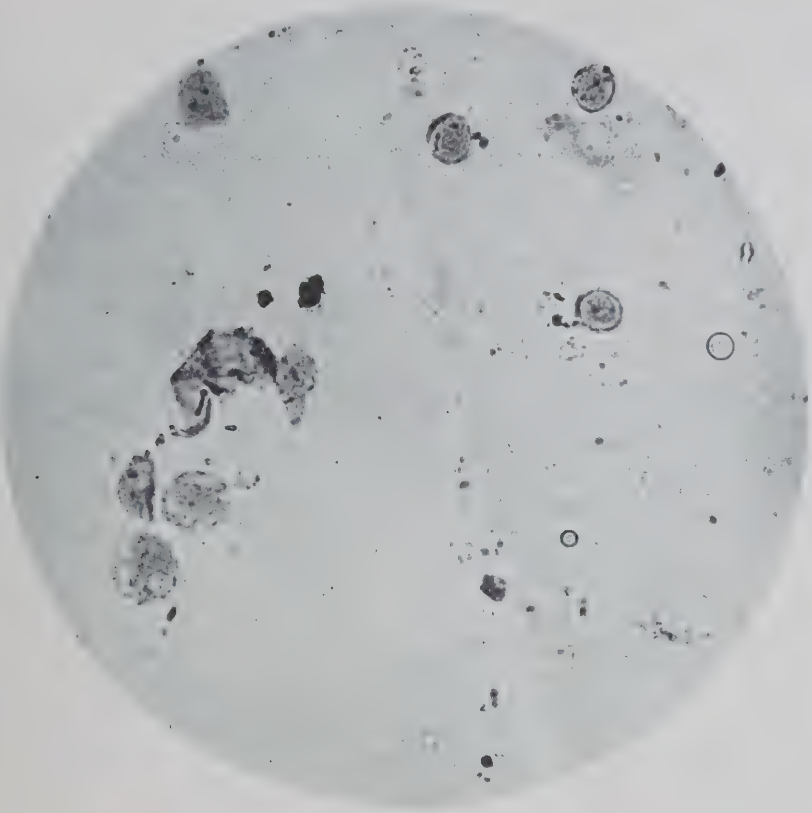

FIGURE 101. SMEAR FROM APEX OF A TOOTH WITHOUT A FISTULA.

We would, accordingly, restate the fundamental, which has generally been thought of about as follows: namely, *that flowing pus from a fistula is necessarily very dangerous to the patient,* to the following:

> **Since an adequately active defense against a dental infection produces a vigorous local reaction with attending extensive absorption, and the products of inflammatory reaction—namely, exudate and plasma in sufficient quantity to require an overflow, usually spoken of as pus from a fistula—this overflow may be, and usually is, evidence of an active defense and is constituted almost wholly of neutralized products, and is often sterile; and such a condition is much more safe than the same infected tooth without such an active local reaction.**

CHAPTER XIV.

EFFICIENCY AND HARMLESSNESS OF ROOT CANAL MEDICATIONS.

PROBLEM: Can infected pulpless teeth be readily sterilized by root medication?

EXPERIMENTAL AND DISCUSSION.

A search of the literature of the dental profession reveals the fact that for seventy-five years there have abounded formulas which were considered competent to sterilize infected teeth. Practically all authors, prior to the last decade, seem to have taken for granted that teeth properly treated were rendered sterile. A criterion that seemed to be dependable—namely, the comfort of the teeth—seemed to guarantee the success of this operation since infected teeth were expected to become painful and abscessed if they were not completely sterile. The relatively small percentage that did become painful were interpreted to constitute the group that had not been adequately sterilized. This research was undertaken to establish, by means of experimental data, the soundness of that conclusion, and with the full confidence that the experiments would corroborate and establish the general presumption to be a fact.

Figure 102 shows a series of roentgenograms of the same tooth, treated by me in 1901, at which time I sterilized the tooth according to the regulation methods of the time; and in accordance with the roentgenograms, since the periapical area diminished and there was apparent deposition of bone with a condensing of the bone about the apex, I seemed justified in concluding that my operation had been a success, since I put in an up-to-date root filling extending to the apex. Owing to the patient's having a progressive type of deforming arthritis, I later, in 1916, sent for her and on the strength of our accumulating experience extracted this and some other teeth. Note that the bone, as shown in A, B, and C, had become continually more dense about this tooth. Upon its extraction, and at which time it was not in the least tender, nor had it been since its treatment fourteen years previously, cultures were made at the apex of the tooth, internally

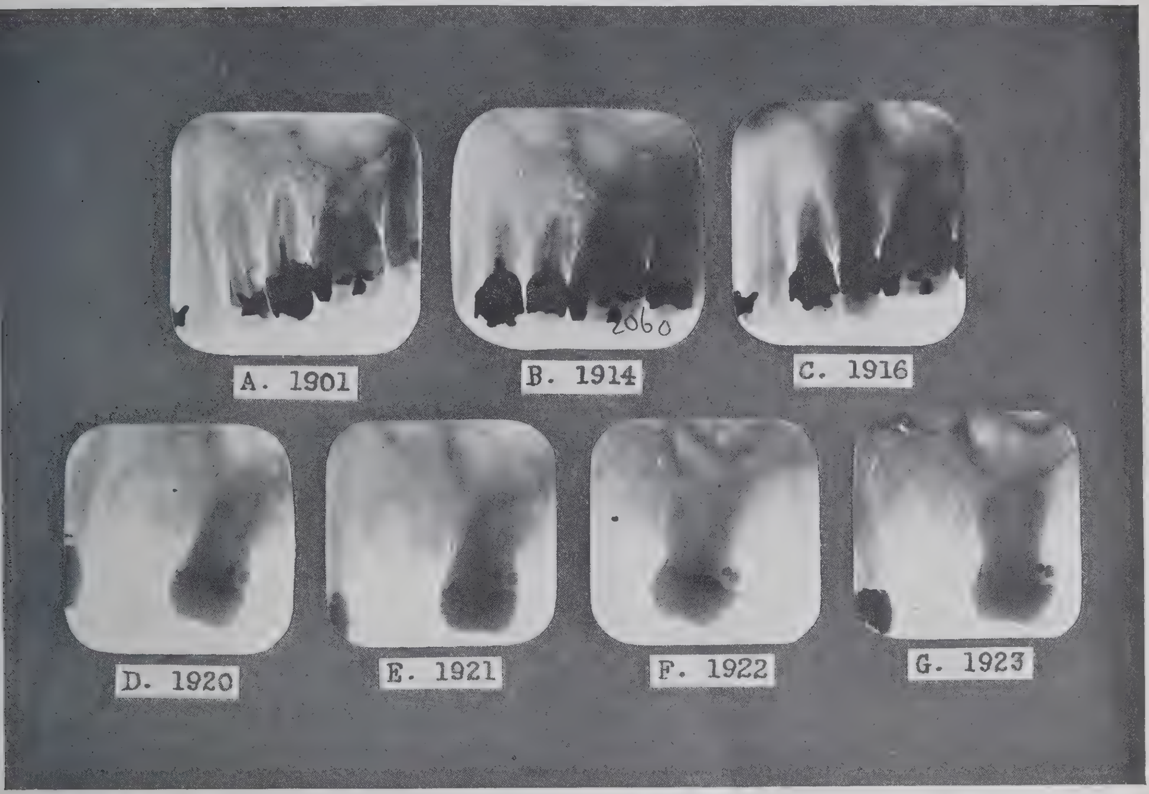

Figure 102. Changes in radiolucency about same tooth, second bicuspid, in fifteen years. Patient has deforming arthritis. A, taken in 1901, B in 1914, C in 1916. Return toward normal after extraction shown in D, 1920, in E, 1921, in F, 1922 and in G, 1923.

and externally. Before extraction a curetting was made to the bone at the gingival margin with an actual cautery, and the tooth was found profusely infected with a strain with definite tissue affinity qualities; and more, not only was the root infected through and through, but the bone for considerable distance about the tooth, as reported in Chapter 3.

Because of many experiences corresponding to that just cited, we planned a series of experiments that were intended to demonstrate why we failed in such cases as the above. One of the earliest tests was to place in the roots of teeth sterile root dressings, carrying various medicaments which were left sealed in the root for various periods of time. This first series was all done on patients; and to our complete amazement, in practically all dressings that were left in roots forty-eight hours, and with most of them after twenty-four hours, the apical third of the dressing was found infected regardless of what the medicament was that was placed on that dressing, *provided there was an apical involve-*

ment about the root. These studies suggested that there was a quantity effect that was very important: namely, that we were not able to put into the root of a tooth, sufficient medicament to overcome the nutrient effect of the fluid within the tooth, and surrounding the tooth, regardless of the medicament. We accordingly tested the relation of tooth mass to medicament volume, by placing blocks of infected tooth substance in relatively large quantities of medicament, and found that, in over a hundred medicaments and dilutions of same even under the very unusual conditions in which a large mass of medicament was in contact with both the inner and outer portion of a section of tooth root, and where medicaments of strengths were used which clearly would be prohibitive in the mouth, because of their destructive action on the adjoining vital tissues the cementum and dentin were not disinfected except with a very few medicaments: namely, formalin in all strengths, iodin 5%, and chlorophenol. It was found, however, that many medicaments exerted inhibiting effects where organisms often grew out days or weeks after being transferred from the medicament to culture media.

The next series of experiments was made to determine the ability of medicaments to maintain the sterility of the root-dressing when sealed in an infected root and without the perforated root-apex's being immersed in an infected culture medium. The medicaments found most promising in the preceding experiment were used for these tests: namely, formocresol, iodin-creosote, iodin 7%, formalin concentrated, phenol 5%, cloves 50%, sulphuric acid 50%, thymol, mercurophen, chloralhydrate, hydrogen dioxide, creosote, alcohol 70%, chlorophenol, phenol compound, chlorazene 4%, dichloramin 15%, and phenol saturated. In these it was found that the most radical disinfectant was dichloramin-T used in saturated form; but in this strength was found to be exceedingly irritating when used in conditions of the mouth, often producing great pain and irritation of the supporting tissues. At that time we made a note: "The members of the profession are warned never to place the 15% or even a 5% solution of the Dichloramin-T in oil of Eucalyptol, its solvent, in any tooth or on tissues."

Of the 18 medicaments used for this experiment, only 6 gave instances of negative results in cultures; or, in other words, were efficient; the remaining all gave positive cultures in every case for the complete series of hours run. The five best results are shown

	5 Hrs.	24 Hrs.	48 Hrs.
Dichloramin-T	100%	100%	100%
Iodin Creosote	81%	25%	0%
Phenol Compound	81%	50%	0%
Formalin	75%	94%	37%
Formocresol	56%	62%	6%

in Figure 103.

The next experiment was made to determine the ability of the medicaments to maintain the sterility of the root dressing when sealed in an infected root, when the perforated root apex is immersed in an infected culture medium. For this experiment, forty medicaments which showed the most encouraging results in experiment No. 1 were tested, and the efficiency of the various preparations determined by placing the dressing carrying the medicament in the root canal with its small perforated apex corresponding with the small open foramen, and the tooth so prepared, itself an infected root, was placed in a container in which was placed a small quantity of infected culture media which came in contact with the apex of the tooth, the tooth crown being covered to the cementum, after it was dried, with paraffin. Of the forty medicaments used, only eight gave negative results, the remainder being all positive in every trial and for all periods of time. The length of time the medicament was left in the tooth was found to make a very great difference. This test was not made to determine the ability of the medicament to sterilize tooth structure, but rather the ability of the medicament to maintain the sterility of the sterile J. & J. absorbent point on which it was placed in the tooth. The points were removed under sterile conditions and cut into sections 1, 2, 3, and 4, numbering from the root apex up.

	5 Hrs.	24 Hrs.	48 Hrs.
Phenol Compound	70%	15%	0%
Dichloramin-T 15%	35%	5%	0%
Formocresol	34%	0%	0%
Iodin-Creosote	33%	25%	0%
Iodin U. S. P.	10%	34%	0%
Formalin U. S. P.	0%	34%	0%
Phenol U. S. P.	0%	45%	0%
Oil of Cloves	0%	25%	0%

Figure No. 104 shows the result of the eight best of the forty: All were infected in forty-eight hours, nearly all in twenty-four hours, and a few had some efficiency, if tested within five hours.

Experiment No. 4 was made to determine the ability of medicaments to sterilize infected dentin and cementum when sealed in the root canal, and when the perforated apex is surrounded by infected culture medium, as in the conditions in Experiment 3. Note the difference that in this experiment we are determining the influence on the dentin and cementum; whereas, in the former, we are testing the ability of medicaments even to maintain the sterility of the root canal dressing. After the test was made on the teeth, as in the previous experiment, the teeth were divided longitudinally with precautions to prevent contamination, and cultures were taken with fine-pointed burrs, properly controlled against contamination, from various structures in various parts of the tooth. The results of these experiments were that with the exception of concentrated formalin which showed 93% sterility, all of the teeth showed a general infected condition of the various tooth structures, and even formalin 5% had a very low efficiency.

Tests were made similarly with double salt of ammonium silver and formalin. Four series were run. Series 1 gave an efficiency of 69%; Series 2, 78%; Series 3, 84%; and Series 4, 95%.

The general result of these studies was summed up under "General Summary and Conclusions" as follows:

"1. Infected dentin and cementum are not readily sterilized by medication, even when the amount of medicament is largely in excess of the mass of tooth structure.

"2. The medicament contained in a medicated root dressing very readily and rapidly loses its disinfecting power, for the dressing itself becomes infected in a few hours, even from the infected dentin and without being in contact with an infected solution.

"3. The medicament in the dressing dissipates more rapidly when one end of the dressing is in contact with an infected culture medium, such condition as obtains in a periapical infection.

"4. The efficiency of a root treatment is greater a few hours after it has been placed in the tooth than several days', or even one day's time.

"5. All areas of cementum and dentin are difficult to sterilize, as well as tend to reinfection, when the medicated root dressing is left more than a few hours.

"6. The medicaments that are most efficient, namely, silver nitrate and formalin, are very objectionable, the former by its discoloration and the latter by its destructing and irritating properties, except when used very dilute and for a short time and then quite efficiently.

"7. There is much encouragement in the use of Chlorazene (chloramin-T) and Dichloramin-T products. The latter, however, is exceedingly painful and destructive in over half of one per cent strength.

"8. We now understand why it has been, that if a root treatment is left in the tooth for an extended period of time, it becomes foul in odor. Also a verification of the observation previously reported by one of us, Price, to the effect that medicated root dressings will always show bacterial growth after they have been left in infected teeth for a few days.

"9. These determinations indicate to us that an exceedingly small per cent of the teeth, that have been treated by members of the dental profession in the past, have actually been sterilized.

"10. Nature is, and has always been, very tolerant, and much of the credit that has been taken by, and given to, the dental profession for the sterilization of infected roots, has really been due to Nature for her kindness in tolerating, at least without local irritation, a probably almost universal and permanent condition of infection, though in lessened amount, when tooth structures have once been infected and have been subjected to treatment."

These experiments were made under my direct supervision, partly by myself and partly by an assistant, Mrs. Matilda Moldenhauer Brooks[4] in the Research Institute of the National Dental Association, in which I was Research Director; and a full report will be found in detail, in the Journal of the National Dental Association, Volume V, No. 3, March 1918, pp. 273-303, which report was read before the National Dental Association at its Twenty-First Annual Session, New York City, October 1917.

We have run many controls and parallel experiments, and have found that the one that seemed to give most satisfying results in our hands has been chloramin-T (not dichloramin-T) which can be used in saturated aqueous solution in paste form, is soluble in water up to about 8 to 12% (Dichloramin-T is not soluble in water), does not discolor the teeth, and by being used as a paste, has so much reserve material for sterilizing that it retains its efficiency for a longer time than most of the preparations, and is not particularly irritating unless there be considerable vital pulp tissue within the root. The silver formalin, or the silver precipitated by other means, as for example eugenol, has high efficiency where it can be used, but produces marked discoloration.

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[4] See bibliography.

In addition to the above studies, we have carefully cultured many teeth after we had thoroughly treated them, with the hope and expectation of retaining them in the mouth; but later decided to remove them; and, in practically all cases where teeth had been putrescent and had evidence of periapical involvement, though slight, we practically always failed to sterilize cementum at the apex, and frequently had positive growth from the dentin.

Another phase of this problem has been the checking of the more improved methods of sterilizing infected tooth structures within the mouth, since it has been claimed[5] that by testing the tooth which had been sterilized, it was possible to determine whether or not that process had been complete. It is advocated, for example, by some authorities, that if a canal point saturated with culture medium is placed in the canal after its sterilization, a determination can be made in one, two, or several days, to determine whether or not sterilization is complete. In the chapter on bacterial accommodation we discussed the quality which bacteria have of adapting themselves to environment. In our studies, reported previously, we found that the practise of discarding controls and tests at the end of one or two weeks was entirely misleading, for very frequently the medication had the effect of inhibiting growth completely for a period of several weeks. But this is not the only difficulty. The organisms may, under the stress of the medication, take on a quality which requires an entirely different type of medium, not only differing in nutriment but in oxygen tension, which qualities apparently are not adjusted to, nor is there a report of their having been taken into, consideration in the reports that have indicated that complete sterility might be depended upon, particularly if checked by this simple test.

Another argument that will be made will be that ionization, either by means of ionizing potassium iodide, sodium chloride, or other solutions, will disinfect infected cementum, when applied through the pulp canal. This problem was very thoroughly studied by Pond and Price[6].

We have found strains in treated teeth in the mouth, for which we could not find any medium, on which they would grow until

[5] See bibliography.

[6] See bibliography.

we would place them in a sealed Petri dish, which was connected with another Petri dish by an hermetically sealed tube, in which second dish was growing a culture of an organism which rapidly consumed oxygen. For days no growth would appear, when suddenly it would start, but cease to continue to grow as soon as that optimum of oxygen tension was passed. They would not grow in less or more than a limited range of partial tension, and all our efforts to grow them by regulation methods aerobically and anaerobically completely failed. We now believe that many of our early determinations, where we got negative results, were so only because we were incapable of furnishing the proper medium and environment. We are also sure that this applies equally to some of the negative work of others; and, accordingly, while a positive growth can only be read positive, a negative growth is not necessarily negative.

As we have shown, it is exceedingly difficult to neutralize infected dentin under any circumstances, without using medicaments which may in some degree endanger the supporting structures. Such studies made on extracted teeth are open to the criticism, that the conditions are not the same as in the mouth, and therefore cannot be considered comparable, since we do not have the original tooth in contact with vital tissue. To overcome this difficulty, and to throw further light upon the matter of tooth sterilization, I have planted many teeth under the skins of rabbits to determine their effects upon the animal, before the tooth was medicated, for comparison with the effect of placing within that tooth such medication as is placed in teeth in the mouth. There is a great difference in the effect of different teeth on the rabbits when planted in this way beneath the skin. Frequently they are incysted and the rabbit tissue proceeds to absorb the root. In some others, notwithstanding the incysting, a nephritis is slowly developed, as illustrated elsewhere. In still others, the dental infection or the toxic products from the tooth, or both, completely prevent Nature's effort to encapsulate the tooth, and in many instances the rabbit is dead in from one and one-half to a few days; as, for example, we reported in Chapter 17 a series of over twenty-five rabbits which were killed by a single tooth in from one and one-half to six days, one rabbit living ten days. For this study I have selected teeth, which killed rabbits in from two to four days, after they were extracted from the patient, where, incidentally, there was no roentgenographic evidence that they were particularly serious, though the patient was being systemically injured by them. Some of the results have been as follows:

A tooth which killed a rabbit in three days (R. 1110) was opened through the crown as it would be in the mouth, the pulp canals cleansed and a dressing placed in it of iodin and creosote. The tooth was placed under the skin of another rabbit which died in four days (R. 1115). The tooth was again opened and treated with the same medicament and placed under another rabbit's skin and it died in four days (R. 1119). Inasmuch as sterile teeth produce no effect whatever in rabbits, it is very important to note that this tooth not only killed the rabbits, but that they began losing in weight within a few hours after placing the medicament, and lost approximately twenty per cent of their weight in two days. This amount cannot be due to the dehydration or starvation of the animal, for it goes on progressively till sometimes at the time of the death of the rabbit, it will have lost forty per cent of its weight, and present a condition of marked marasmus.

Similarly, we have tested a number of medicaments by treating the teeth with them before planting them under the skin of a rabbit, as nearly as possible as they would be treated in the mouth. In this way we have tested chloramin-T, silver nitrate neutralized with formalin or eugenol, formocresol, two per cent formalin and hot air, with similar results to those obtained with iodin and creosote as above. I have now made several hundred of these determinations, results of which emphasize the need both for a new appreciation of danger from infected cementum, because of the apparent difficulty, if not impossibility, for sterilizing infected cementum by treating through a root canal. The results so far obtained also stress the great necessity for repeating these tests under as carefully controlled conditions as possible, which we are doing as this goes to press. I will publish further details later.

To determine the nature of radiations of a greater length but still in the ultraviolet range, we have studied the effect of placing a tooth that had proven to be fatal to several animals when placed under the skin, under the radiations from the water cooled mercury vapor quartz arc lamp, and have found a very marked change in the reactions of the rabbits when the tissues over the implanted tooth were so treated. Whereas, this tooth previously produced a very marked leucocytic infiltration about it, there were practically no leucocytes, or very few, the organisms being present in pure culture in large numbers in the exudate of the tooth at the time of the death of the rabbit, and the rabbit had developed a very violent appendicitis and colitis, and probably peritonitis. Whether this change in the effect of the infection after the ultraviolet radiation was due to a change in the attacking power of the organism as a result of this radiation, or to a greater susceptibility of the abdominal viscera because of the depressing effect of the radiation, we are not yet able to state.

But it may be stated, and justly so, that this does not yet produce an experiment which is closely comparable to those under which operations are made in the mouth. To test this still further, I have made the following experiment: A tooth, the right second mandibular molar, with a hypersensitive and degenerating pulp, shown in Figure 105-A, which tooth was considered very valuable to the patient, and which showed slight, if any, alveolar absorption at its apex, was treated with dichloramin-T, put in with good access in the canals for twenty-four hours, and was then root-filled with the result shown in Figure 105-B. Two years later the tooth was extracted and also one adjoining it (the third mandibular molar, the root of which was treated and refilled at the same time as the second molar), as a matter of precaution, since the patient was considered sufficiently susceptible to strep-

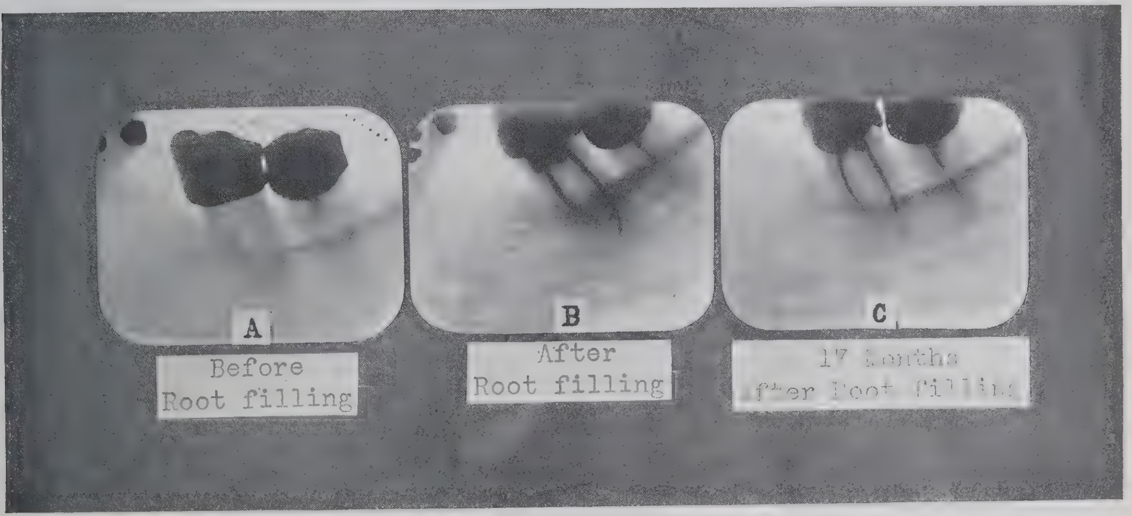

FIGURE 105. THREE SUCCESSIVE VIEWS OF A MANDIBULAR MOLAR. A, BEFORE REMOVAL OF DEGENERATING PULP, B IMMEDIATELY AFTER ROOT FILLING, C SEVENTEEN MONTHS AFTER ROOT FILLING.

tococcal infection to require protection, and because there was still enough sensation to pressure in tapping in the tooth, to suggest that it was not entirely normal, notwithstanding the appearance in the roentgenogram, as shown in Figure 105-C. This tooth was extracted, thoroughly washed in sterile normal salt solution, the root divided, and each part planted beneath the skin of a rabbit. It will be noted that at the time of the root filling, there was a very slight protrusion of the chloropercha to make a so-called encapsulation, but there was every reason to believe that the roots were efficiently treated and well filled, not only because of the method used, but also because of the suggested improvement in the supporting structures of the tooth about the apices of the roots, as shown by the reduced area of alveolar absorption from a small but definite area in B, to no apparent area in C. The effect of these roots on the rabbits was as follows:

To determine whether or not there was infection within the structure of the root, I sterilized the apex of the tooth with a hot instrument, searing deeply, then drilled through the seared structure to the interior, and cultured the chips which grew out a strain of diplococci. After dividing the roots, they were washed thoroughly in normal salt solution, and one was placed with surgical aseptic procedure beneath the skin of each of two rabbits. A purulent infection developed about each, but much more rapidly about the mesial root than the distal. The mesial root killed four rabbits in succession in an average of six days, with an average loss in weight of twenty per cent. The distal root killed two rabbits in thirty days, with an average loss of thirty-one per cent. In another place I am discussing the result of boiling the mesial root, which rabbit is still living, at the time of this writing, forty-six days after implantation and has gained 228 grams, or 21 per cent.

Great care must be taken in interpreting these results; and it is only because of the large number of similar results that I consent to present such a striking case, for I realize fully that many men, who, because of their greater interest in exodontia than in dental pathology, will be in danger of jumping at the conclusion that this is positive proof that all root-filled teeth should be extracted. I do feel it my duty, however, to make this important information public, to aid in crystallizing an appreciation of the danger that may attend an over-confidence in the completeness of the sterilization of infected roots. I will state here what I have stressed in further detail in other chapters, that many parts of the body are exposed to infection, and we have reason to believe contain infective germs frequently or for extended periods; but the condition of safety or danger will be dependent quite largely on the defensive factors of the patient; and with a given tooth, some individuals will, I believe, be relatively safe, while others will be in definite danger. I am not ready to draw the line so rigidly as to state that all root-filled teeth should be extracted for every patient or for all patients in any given time, though I do believe there is a limit of safety for all such teeth for each and every patient. I do deem it absolutely essential that very exhaustive researches be continued on this subject in order that we may be able to draw our lines with greater exactness than we can with the limited knowledge, though very important, that is available. I think I should state here that I have not seen a single logical presentation of data that will justify the claims of any of the extremists, such as the so-called "hundred per centers." In Chapter 17 on Quantity, Systemic Effect, and Tooth Capacity, in Figure 122, I present a table showing the results of 237 implantations 209 of which were teeth, which should give much food for thought for those who believe that comfort and roentgenographic appearance are a guarantee of the absence of tooth infection.

I have made many tests, and have many in progress, to determine whether, and by what means, infected teeth may be completely sterilized by treating through the pulp canal where there had been definite evidence of destruction of the peridental membrane about the apex. In Figure 106 (R. 1149) there is shown a rabbit that died in two days with a loss in weight of seventeen per cent, from a tooth that had been treated with silver nitrate neutralized with twenty-five per cent formalin, by placing these within the pulp canal, but without allowing these medicaments to get in contact with the cementum. A shows the tooth under the skin and an abscess as big as several silver dollars, with pure culture of streptococci, as shown in B, and which I believe grew out from the infected cementum, which infected cementum was not sterilized by the silver nitrate neutralized with twenty-five per cent formalin. Similarly, I have passed fuming formalin (forty per cent formaldehyde) through the pulp canal of an infected tooth, where I had reason to believe the cementum was also infected, and in which I protected the external surface of the tooth by putting a rubber dam on both the neck and the apex. This material passed through the tooth with a gravity pressure

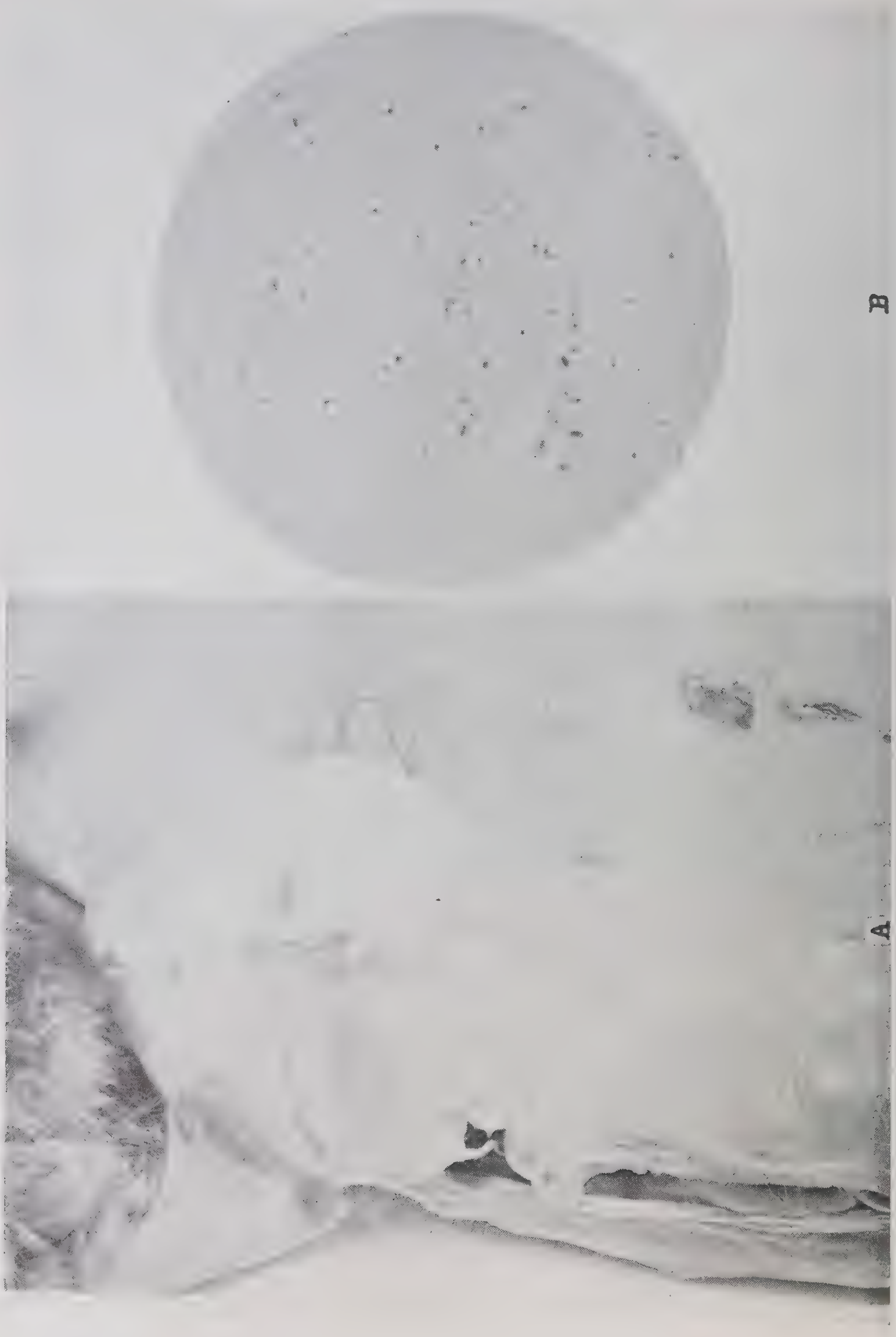

FIGURE 106. RABBIT APPARENTLY KILLED BY THE INFECTION IN THE CEMENTUM OF AN IMPLANTED TOOTH, AFTER DENTIN WAS TREATED WITH SILVER NITRATE AND FORMALIN.

of about one-tenth of an atmosphere for fifteen minutes. The tooth was then washed with normal salt solution, also irrigated through the pulp chamber. Ten grams of the concentrated formalin passed the tooth. After washing, an effort was made to remove all trace of formalin by passing a stream of air through the pulp canal, the apex of which was sufficiently large to pass a considerable stream. The tooth was then planted under surgical conditions beneath the skin of a rabbit, and an abscess developed containing pure culture of diplo- and strepto-cocci. It seems probable that the fire-wall existing between cementum and dentin was not penetrated by even concentrated formalin in fifteen minutes' time in sufficient quantity to destroy the organism within the cementum. Much light is thrown upon this problem in the subsequent chapters on Chemical Changes in the Blood and The Nature of the Defensive Factors in the Blood and the Forces which Injure Them.

In the physical structure of the tooth with the dentin connected chiefly, if not solely, with the pulp, and the cementum connected chiefly, if not solely, with the pericemental membrane, we are dealing with two structures, each sufficiently porous to give habitation to millions of organisms. We have shown elsewhere that the dentinal tubuli of a single rooted tooth comprise enclosed canals totaling approximately three miles of length, and it is probable that no dental canal exists too small for organisms to develop within it, but each of these two structures is formed on a practically continuous homogeneous base, the dentin and cementum being backed up to each other. Whether, as believed by some, there are communicating channels from the lacunae and canaliculi of the cementum through the dentino-cemental boundary into the dental tubuli of the dentin, or whether the only communication between these two structures will be through multiple foramina, is not yet definitely established, though several conditions suggest one or the other of these answers to be correct.

In order to throw light upon this important problem I have placed infected teeth, as they were extracted, in culture media sufficiently hardened with agar to localize the bacterial growths, and have found that the bacterial growth in the medium seems to be entirely limited to zones which are probably foramina of the tooth, chiefly apical with some lateral. I have similarly tested this same problem by placing within the teeth, solutions, the ions of which, when they would pass by osmosis from the tooth to the agar media surrounding the tooth, would react on the coloring medium by the change in the pH. These have also indicated that for all practical purposes a very large proportion of the total communication is limited to the foramina. In Chapter 23 we have shown that the structure forming the boundary between dentin and cementum, is in effect a dialyzing membrane, and that electrolytes may pass through that membrane quite freely while colloids cannot. It is, accordingly, very probable that certain crystalloid substances can pass through this boundary.

SUMMARY AND CONCLUSIONS.

It should be remembered that in the formation of the tooth, both the dentin and cementum are built upon a first zone of calcification which is in effect a continuous fire-wall or protecting zone between the two structures, with but relatively few direct connections or openings from the dentin to the cementum. In the structure of the dentin, with its long and narrow channels constituting the dental tubuli with their anastomosing branchings, we have a structure, particularly favorable, for the hiding away of the organisms because of the mechanical difficulty of getting medicament into the structure. We think it is probable that often a relatively high efficiency may be secured in sterilizing young dentin to the granular layer, and possibly to the dento-cemental junction. We think it is very improbable, from our many experiments, that the cementum can ever be sterilized by a medicament placed within the pulp chamber, without definitely and seriously embarrassing the surrounding supporting structures.

We would, therefore, change the accepted fundamental from *That infected teeth can be sterilized readily by medication, and that the usual medications do not injure the supporting structures*, to

> **That infected teeth can be sterilized in the mouth only with very great difficulty or by using over strong medicaments; and the usual medications (particularly those previously used) frequently, if not generally, injure to some extent the supporting structures.**

CHAPTER XV.

ROOT FILLINGS, THEIR CONSTANCY AND EFFICIENCY

PROBLEM: Do root fillings fill root canals, and do they continue to do so?

Practically all diagnosticians, whether dental, medical, or otherwise, who look at roentgenograms of the teeth, look to see whether there is evidence of more or less bone destruction at the apex, and if so, whether the tooth carries a root filling. If it does not, it is like a bottle filled with infection; if it carries a root filling, there is no opening in the bottle, provided the root filling goes to the apex. What could be more simple, complete, and fortunate?

This particular study was undertaken to establish some of the mechanical problems involved: First, under what conditions is it mechanically possible to fill pulp chambers? Second, what is the constancy of the physical state of the mechanical plug we insert? And third, what are the physical properties of the materials used for root fillings?

My work on the physical properties of the waxes, used for impressions and patterns for prosthetic and inlay work, revealed the following important factors:[7] First, that most waxes have a wide range of variation in volume in proportion to their temperature; and second, that practically all waxes have a property of elasticity. Every person who has poured paraffin, tallow, lard, beeswax, or such substance when liquid and molten with heat, into receptacles to cool, has observed that, on cooling the center became depressed and, finally, with the last cooling, a great open crater ran down into the mass of the material, often to the bottom of the vessel, with branchings in various directions. At this stage, 5 to 10 per cent more material could be poured into the form filling these cracks before bringing it to the original level of the molten mass; and when this mass cooled, it again, in the same proportion, had its shrinkage, and so on indefinitely. Fundamentally, with a change of state, there was a definite change in mass.

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[7] See bibliography

Since heat was formerly used a great deal in packing gutta-percha root canal points, the problem arises, "To what extent does the same factor obtain?" All who had experience in the use of chloropercha, as it was used so extensively years ago for root fillings preliminary to placing the points, had a practical demonstration of the effect of leaving the stopper out of the bottle, with the result that the bottle containing, say a half ounce of creamy chloropercha would, after evaporation of chloroform, leave a nugget that was always drawn away from the sides of the bottle, and which would rattle about with great freedom. In discussions and questionings regarding the possibilities of this condition's obtaining in the mouth, I was always assured that the two conditions were not comparable.

For references to some of the detailed work that I published on the relation of change of state to mass, of various substances including molten gold, I would give the following: Price[8]—The Laws Determining the Behavior of Gold in Fusing and Casting—Dental Cosmos March 1911; Special Researches in Physics—Journal of the National Dental Association, October, 1914; and the reference to my previous publication on this subject in the Journal of the National Dental Association, December, 1918.

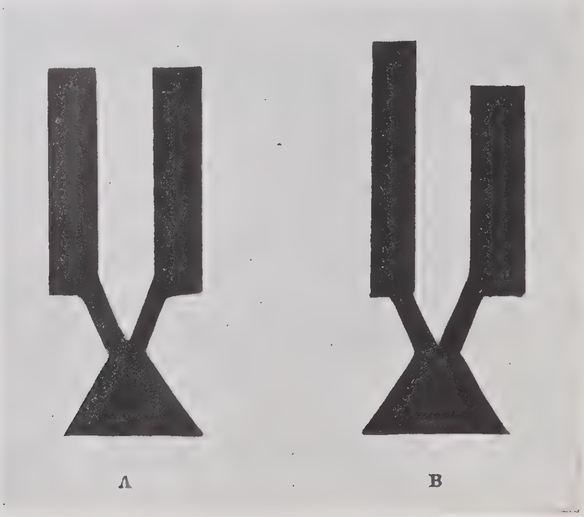

Figure 108. Two similar wax bars placed in a warm investment and cast. A, before heating, B after heating and while investment was still soft, showing the changes in the wax and the shape of the casting.

From the latter I take the following illustration. Figure 108 shows similar wax bars placed in a warm investment and cast: A, in wax before heating by putting in the warm investment; and

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[8] See bibliography.

B, after casting showing the change that has taken place as a result of the heat. This is neither expansion nor contraction; it is the releasing of elasticity. A wax bar was warmed, and while sufficiently warmed to compress, the pencil of wax was put under pressure on end, which shortened it. In changed state under pressure it was chilled. Another cylinder of the same wax was treated similarly, except that it was stretched instead of condensed. From each, sections one inch long were taken. These two wax bars were similar in every respect, except that one had a retained elasticity in one direction, and the other in the opposite direction. When the two pieces of wax were placed in the warm investment, the warmth released the retained elastic stress; and after the retained elasticity was released, the compressed piece became longer and the stretched piece became shorter. This took place in the investment which was heated just enough to follow the changing wax, with the effect that before the wax was melted from the investment, two entirely different sizes of molds had been formed. Since both were attached to the same sprue-gate, and both were cast together, the castings reproduced this physical change which took place in the wax. It also followed its own law of contraction, and all diameters were reduced in accordance with its laws of contraction.

In the former of the articles just referred to, I showed that pure gold changed approximately 2 per cent in mass, within a fraction of a degree, in changing from the solid to the liquid state, and approximately another 2 per cent in changing from its first crystalline form as it freezes to room temperature. These are cubic measurements, linear being one-third of this amount. Ice behaves differently by changing in the opposite direction, which is the reason pipes and bottles burst. Our waxes, gutta-percha, etc., when placed in root canals, behave in the opposite manner to that which water does when taking on the solid state, and change to a greater degree, ice being 11 per cent greater in volume than water at the freezing point. To test these dimension changes cylinders of glass were used, and the gutta-percha packed with all pressure the cylinders would stand at various temperatures, and these, when cooled, were tested for the filling of the chambers by placing ink in the cylinders, which invariably passed in between the gutta-percha and the cylinder walls; and, indeed, it was a physical impossibility so to pack the gutta-percha at a temperature at which it could be molded, that there would not be a space between the gutta-percha and glass when the gutta-percha had cooled. Several hundred pounds' pressure were used on the gutta-percha without avail, and, notwithstanding that the pressure was kept on the gutta-percha while it was cooling (which could not be done in a tooth), this shrinkage took place. Figure 109 shows a typical tube demonstrating this effect. The metal pistons are shown continuing the pressure of several hundred pounds on the gutta-percha, notwithstanding which, the gutta-percha left the glass sufficiently to let the ink flow between.

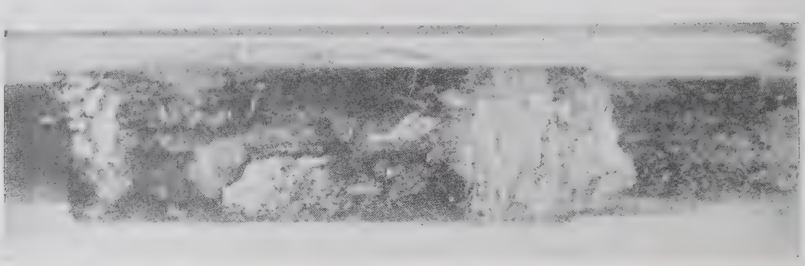

FIGURE 109. GUTTA-PERCHA UNDER A HIGH PRESSURE INSIDE OF GLASS TUBING, TO TEST THE SHRINKAGE OF COOLING GUTTA-PERCHA. NOTE THE INK FLOWED FREELY INTO THE SHRINKAGE SPACE.

However, it is not considered feasible to make gutta-percha moldable in root-filling procedures by means of increasing its temperature. This is done by placing it in a solvent, usually chloroform or chloroform carrying rosin, and the use of oil of eucalyptol as a solvent. Gutta-percha dissolved in chloroform to a consistency of a thick cream or paste, has a volume 300 per cent greater than that of the original material; or to express it otherwise, if the pulp chamber is filled with gutta-percha at about that consistency, when the chloroform has evaporated from it, the chamber would be approximately one-third full. If we put into the creamy mass a cone of dense gutta-percha, the usual gutta-percha point used in root filling, and select one which fills the chamber within 90 per cent of full, leaving only 10 per cent of the volume for the chloropercha, the chamber will still lack 6.6 per cent of being full, when the chloroform has volatilized. Doubtless, many operators have supposed that, merely softening the point with chloroform to make it flexible and moldable, would not change its volume, which is not correct. A sufficient quantity of chloroform to make the gutta-percha flexible is sufficient to change its mass very definitely as will be shown. Gutta-percha, when dissolved with chloroform, makes a sticky paint; but when the chloroform is gone, it peels from all smooth surfaces in its process of contraction and does not retain adhesiveness. It was doubtless for this reason that Dr. Callahan sought another substance, suggested and used rosin; and doubtless for this reason, and for the advantage of a non-irritating sterilizing medium that Dr. Buckley suggested eucalyptol as the solvent for gutta-percha. The ultimate contraction is very great for both of these substances, and corresponds ultimately, relatively with the amount of solvent used, whether the solvent be chloroform, eucalyptol, or chloroform carrying rosin.

The gutta-percha in oil of eucalyptol, the eucapercha of the market, has a volume 417% greater than the volume of the gutta-percha alone, which means that a pulp chamber, filled with eucapercha and submitted to long and complete drying, would ultimately have 24% of the total volume of the pulp chamber filled. When it solidifies, it does so into a lumpy, curdled mass which does not adhere to smooth surfaces. It, however, very fortunately, undergoes this drying process slowly. After weeks of spontaneous air drying at room temperature, it reduced to 87% of the original volume. During a similar period, gutta-percha and chloroform would have diminished to 76% of the original volume. However, by the addition of artificial heat equivalent to that furnished by the body, the rate is greatly hastened, as shown by the tables; but it is not hastened by moisture.

Rosin and chloroform mixture also undergoes a very great reduction in volume, starting with a fluid about the consistency of a light oil. Dr. Callahan suggested a consistency of sewing machine oil as best. In this condition it has a volume 406% of that of the volume of rosin. In other words, a pulp chamber filled with rosin and chloroform solution of that consistency would ultimately be about 24.6% filled. Again, using gutta-percha cones to occupy, say 90% of the total volume, would ultimately leave approximately 7.5% of the pulp chamber unfilled when the complete drying out process has occurred. However, the gutta-percha point will rapidly take up the chloroform and swell so that it will occupy more space, readily swelling to increase in volume ¼ to ½ in the softening process. Since the pulp chamber can contain only a given amount of material, whether fluid, semifluid, or solid, it is a physical impossibility to put in material to make up for the evaporation of the solvent, while the solvent is present. "It is, therefore, a physical impossibility completely to fill a pulp chamber with gutta-percha made plastic by any of the above solvents, except at the time the gutta-percha contains the solvent."

The chloroform and rosin compound has very distinct and favorable qualities, in that it is very adherent and tenacious in all stages, to both smooth and rough surfaces. In this respect, it is unlike each of the preceding compounds. The result of this quality is that, when a root filling is made of this material and gutta-percha cones, the contraction tends to express itself in a large part, by a shrinking towards the walls if dry, rather than as a continuous disc at the side of the mass, and between it and the wall, and herein lies the great virtue of this material as a means for filling pulp chambers.

It will be a matter of surprise, doubtless, to most of us to find that a skin is formed on the surface of each chloropercha, and rosin and chloroform, particularly the latter, which quite effectually delays the drying-out process. In a case of the chloroform and gutta-percha in a narrow chamber, this skin or film separates from the vessel or container, leaving a fault, which ultimately makes a series of caverns, each projecting from the last until the entire mass is honey-combed. In large chambers it contracts to a central free mass. Chloroform and rosin in a narrow chamber of the same form retains the continuity of the protecting surface skin by its adhesion to the wall, and underneath this film the liquid retains a fluidity nearly that of the original, due to the control of the vapor tension by this membrane. Consequently, it is not only a matter of weeks, but of many months, before our root fillings, inserted with any of these three compounds, will have attained their maximum contraction. After air drying in an open vessel for two weeks, rosin-chloroform had reduced to 65% of its original volume; in five weeks to 59%; eight weeks to 36.4%, and the last 12% of the total shrinkage requiring either a long period of time or the addition of artificial heat nearly to the boiling point of water for many hours. When we consider the great variety of forms of pulp canals and the variations in size, shape, and direction of the many foramina, it is evident that the root filling material must seal these foramina by a process of retreating while retaining a close adhesion to the surface of the foramen, instead of contracting to a common center of the mass, producing a fault or space. An illustration of some of the difficulties encountered in root canal fillings is shown in Figure 110. Many other cases are shown throughout this volume, as for example, in the following conditions:

It will clearly be seen that there are many conditions which would make impossible the placing of a large percentage of gutta-

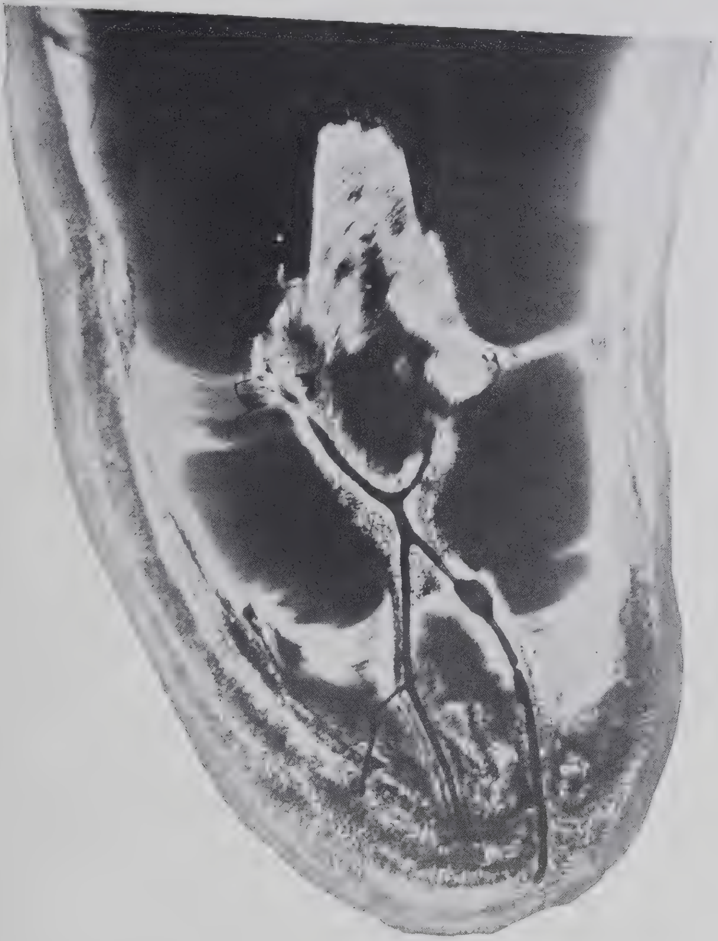

FIGURE 110. SHOWS THE MULTIPLE FORAMINA, BRANCHINGS, ENLARGEMENTS, AND CONSTRICTIONS IN THE ROOT APEX.

percha in the root filling, because of physical conditions: for example, in fan and wedge-shaped canals. No gutta-percha points are made fan-shaped. They are conical. Nor are they made wedge-shaped. The balance of the chamber, that cannot be filled with one or more of the conical points, will be filled with the solvent used; and in case of a lateral canal or several of them, it would clearly be impossible to work the hard gutta-percha into a cross canal, and particularly to make it fill the enlarged opening which many of the foramina have in the cementum.

In general, it may be stated that the amount of ultimate contraction will be the amount of solvent present, assuming that the pulp chamber was filled completely with the root filling and its solvent. The problem of the content of dentinal tubuli will be taken up in a subsequent chapter.

A large number of studies have been made of our own efforts at root-filling, to determine whether or not we had succeeded in filling the roots, and whether sterile teeth, when filled by us under ideal conditions outside the mouth, would remain sterile if placed in an infected culture medium; and in most instances, organisms were found in the tooth structure, in or beside, the root-filling material, or both, in a few weeks' time, and practically always after a period of a few months. Some of these studies are reported in detail in one of my articles referred to above. To assist me in this work, I engaged the service of Dr. Dayton C. Miller, Professor of Science, Case School of Applied Science, who made volumetric tests with a high degree of accuracy. The following are Dr. Miller's general remarks:

"The first noticeable fact in the experiments was the extreme slowness with which evaporation proceeded under spontaneous air drying. It would have required a year, or more, for the materials in the jar to have solidified. Even when heat of 70° C. (169° F.) was applied, the process was not much accelerated. A temperature of boiling water was required, and this was sufficient to melt the rosin and to soften the solid gutta-percha.

"It is not improbable that the rate of drying in a tooth cavity, the walls of which are more or less porous, would be different from that in a glass jar. It is possible that the body fluids may affect the rate; but experiments show that the placing of the material in water does not assist hardening, but rather prevents it.

"A conspicuous physical property of the materials is the great contraction in volume, the final volume in one instance being less than a fourth of the original volume.

"Both of the gutta-percha materials not only contract in volume, but in doing so they fail to adhere to the surface of the jar, leaving it clear of protecting covering, and the materials become porous or granular in structure. It would seem that these properties would render the materials useless for the filling of root cavities. As an illustration it may be assumed that root canals have diameters varying from 0.001 inch to 0.015 inch, that is from 0.025 millimeters to 0.375 millimeters, and that bacteria may have a size varying from 0.0005 mm. to 0.005 mm. The possible contraction of fluid gutta-percha root-filling material in the smallest root canal may be 0.005 mm. while for a large canal it

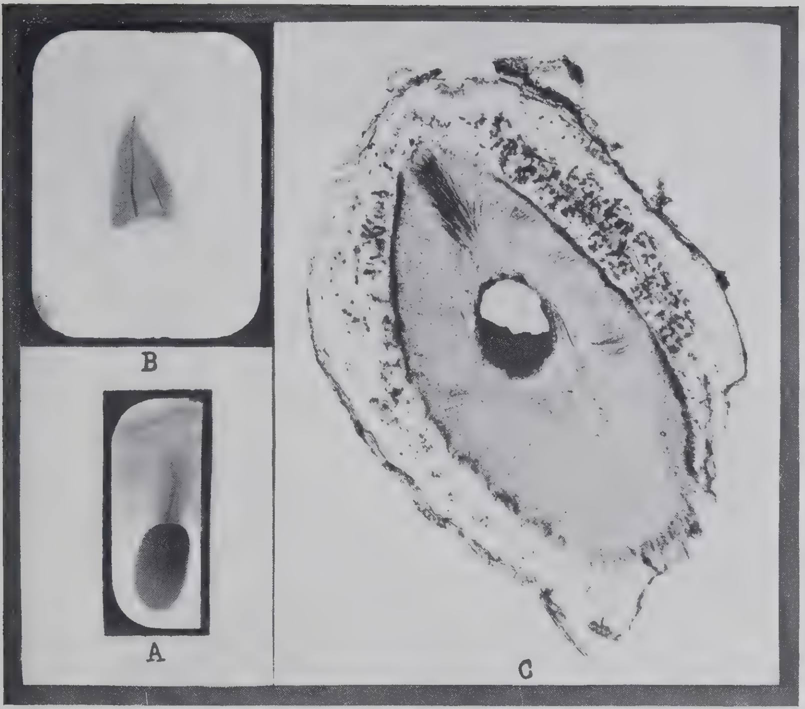

Figure 111. Root canal filling shrinkage. A as roentgenographed in the mouth, B after extraction, C a cross section of the tooth and root filling.

may be over 0.075 mm.; these contractions are much larger than the sizes of bacteria. While these statements of the contractions are not exact because of the uncertainties in the manner of drying, yet it is certain that there will be little protection against the entrance of bacteria.

"The rosin solution when drying differs from the other in that a solid coating remains tenaciously adherent to the whole inner surface from which the fluid has receded, and the solid does not at any time part from the walls. Thus the whole inner surface of the cavity remains protected, and no cracks are left where bacteria may enter through the small canal. There is an inner hollow space, but it is wholly surrounded by the painted walls, and closed at the bottom by the solid.

"These conclusions, however, are not final in regard to the filling of teeth for the conditions in a living tooth are certainly different from those in the glass jar. But the facts of physical contractions, etc., are exactly the same in the two cases."

It is clearly evident also, from the clinical data available, that root canal fillings do not continue to fill the roots of teeth with as high a degree of efficiency, as is generally supposed. Figure 111 shows one of these root fillings, which in the original roentgenogram of the tooth in the mouth, gave the appearance of filling the canal. A shows a roentgenogram of the tooth in the mouth; B, a roentgenogram of the tooth after extraction, showing the mesiodistal appearance which, of course, could not be taken in the mouth; and C, a cross-section of the tooth above the branching.

These studies of the underlying fundamentals indicate how much more difficult it is to fill root canals mechanically than is generally supposed. If, however, a tooth is root-filled, which is surrounded by a non-infected vital membrane throughout its entire cementum, it will doubtless be very difficult for organisms to enter even unfilled dental tubuli, provided they are thoroughly sealed, if such is actually accomplished with chloroform and rosin at the pulpal end of the tubule. If, however, the dentin about the apex is denuded and infected as part of the apical and pulpal involvement, it will doubtless be more readily possible for that ininfection to gain entrance to, and infect, the dentin because of the continuous anastomosis. It is accordingly probable that favorable teeth, whose dentin is infected, but whose cementum is not infected, and has normal attachment, may have from ninety to ninety-nine per cent, possibly more, of the organisms destroyed by medication with Chloramin-T without considerable injury to the supporting structures, and that such teeth can, under most favorable conditions—namely, direct access, a round canal without islands, bays, or fan-shaped channels—be filled so that the great majority of the tubuli are sealed at their pulpal ends and the pulp chamber filled to within a few per cent of full the first few weeks, a larger per cent of unfilled space developing with the succeeding months with an ultimate space in even the most favorable root fillings adequate for the housing of many millions of bacteria, which, if they may find access to such an area, will be sufficient in quantity to do definite damage to the host, provided that individual's defensive activity against that organism is not sufficiently high, a matter which will be discussed in detail in subsequent chapters.

In the preceding chapter under the discussion of the efficiency of medication I have reported the result of planting the roots of a tooth beneath the skin of a rabbit, which had been as thoroughly root-filled as an unusually skilled operator was capable of doing after treating the teeth by a process which is proven to be as efficient as any we have available. The placing of these supposedly sterile teeth, which presumably could not because of their root fillings again become infected, underneath the skin of the rabbits, produced results which indicate that they were not sterile, and were not free from toxic irritation. That this was true, was further demonstrated by drilling into these roots and culturing after sterilizing the surface.

As a part of the daily routine of our research, extracted teeth, which are suspected of being related to systemic conditions, are cultured, some by crushing the root tip or the whole tooth, many by sterilizing the surface and drilling into the tooth structure with a sterile drill and culturing the chips, some by sterilizing the external surface and culturing the tooth. Of the last thousand teeth, less than one-tenth of one per cent of all of our root-filled teeth so tested, failed to grow a culture of streptococci.

SUMMARY AND CONCLUSIONS.

When we consider how many thousands of the extracted teeth we have cultured and found to be infected within the tooth structure, and the extremely low percentage, practically zero, in which infection was not demonstrated, together with the fact, that so many teeth with excellent root fillings, show structural changes of the supporting tissues after a few years have elapsed, we are led to believe that we are dealing in these cases with one of the clinical expressions of the physical facts we have just been studying.

We are, therefore, though very reluctantly, compelled to change our original premise which provided that, *good root fillings fill pulp chambers and continue to do so indefinitely*, to the following:

> **Root fillings rarely fill pulp canals sufficiently perfectly to shut out bacteria completely. Root fillings usually fill the pulp canal much less perfectly some time after the operation, than at the time of the operation, due to the contraction of the root-filling material. The ultimate volume contraction of the root filling is approximately the amount of solvent used where a solvent is used with gutta-percha as a root-filling material.**

(Note:) It is not proven that it is absolutely necessary that teeth be perfectly sterilized or that they be perfectly root-filled in order that an individual may not develop systemic involvement, since under favorable conditions the patient may provide an adequate defense or quarantine against these materials.

CHAPTER XVI.

COMFORT AND SERVICEABILITY AS SYMPTOMS.

PROBLEM: Are local comfort and efficiency of treated teeth an evidence and measure of the success of an operation?

EXPERIMENTAL AND DISCUSSION.

Clinical diagnosis as a science is based upon symptomatology. If we were to ask the question of the dentists, oral surgeons, and physicians of the country, the great majority would give the affirmative answer to the above question; as would also nearly 100 per cent of the laity. The special research on this problem has been undertaken to determine the relationships between symptomatology, clinical pathology, and tissue pathology. The approach has been made in three ways: First, by comparing the history and symptoms with the presence or absence of evidence of systemic involvement; second, by comparing the history with the local histopathology; and third, by tabulating a large number of cases to determine the type of condition which, when obliterated, produced a change in systemic reaction, including both the groups of disturbances with and without evidences of local discomfort.

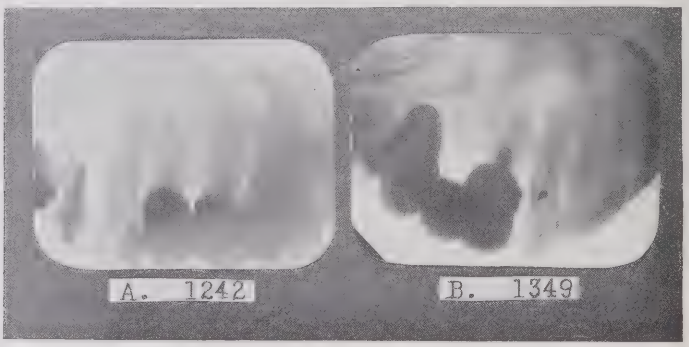

FIGURE 112. INFECTED LATERALS WHICH HAVE GIVEN FREQUENT AND SEVERE DISCOMFORT.

Figure 112 shows roentgenograms of teeth of individuals that reported either continual or frequently recurring tenderness of the teeth here shown. The lateral in A has been crowned for some years, with recurring acute tenderness and finally with a violent abscess which produced extreme discomfort and swelling.

B shows a similar lateral which has a partial root filling, as has also the cuspid. The lateral has had recurring apical abscesses developing for a long period, the tooth becoming very severely inflamed with each recurrence.

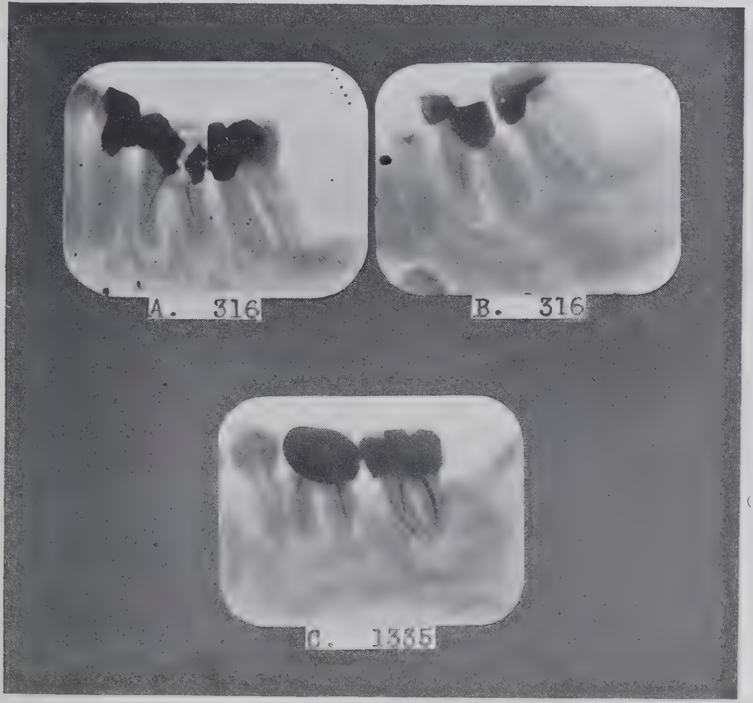

FIGURE 113. TEETH FORMERLY WITH FISTULAE AND RECURRING TENDERNESS, LATTERLY COMFORTABLE. ALL BADLY INFECTED.

In Figure 113, we have roentgenograms of the teeth of a group of cases with the following history: For a more or less extended period of time these teeth were, on recurring occasions, tender or had what the patients termed gum boils. Sometimes this changing condition extended over a period of years, and finally the teeth ceased to become tender. In A the tooth had a fistula which would occasionally close; the tooth would become tender; the fistula would open, establishing free discharge into the mouth; and the tenderness would subside. We insisted upon the removal of this tooth. The patient always delayed the operation and finally stayed away a couple of years for fear we would carry out the program. Finally the fistula closed; the tooth ceased to become tender; and the area of absorption became smaller as shown in B. The patient began to develop symptoms of rheumatism and consented to its removal. The rheumatic symptoms were relieved.

Figure 113-C shows a lower right second molar filled many years ago, and previous to about three years ago very frequently gave the patient trouble, with tenderness and some swelling. About that time she contracted "Flu" which was complicated with a lung involvement and also with a heart involvement, which latter kept her in bed for most of a year, and she was an invalid for a year and one-half. During the time of her attack with "Flu" and the subsequent lung and heart complications, and also since these latter had subsided, since she had had no tenderness whatever in this tooth, she had come to the conclusion that there was no need for its extraction, a matter in which her dentist concurred notwithstanding he had a roentgenogram and knew the history.

In another chapter (Chapter 60) I discuss the relationship between the susceptibility to heart which this lady inherited, five of the relatives on the father's side, including her father, having died in middle life with heart involvement; and in the chapter on the relation of condensing and rarefying osteitis, I have discussed the significance of the zone of condensation, which appears in this roentgenogram, and its relation to this clinical history. (Local Structural Changes. Condensing around Rarefying). The facts are very clear, that during the period when this tooth was giving serious and frequent local disturbance, the patient was relatively more safe, than in the later period during which it gave no response and was for all intents and purposes a normal tooth. The reason for this is discussed in the chapter on the nature and significance of local reaction.

In Figure 114 we have a group of crowned centrals showing even greater areas of pulp canal unfilled, which, according to the history, have never been uncomfortable, and the patients were able to eat with them without thought or consideration. A presents the roentgenographic appearance of the teeth of a middle aged man who was suffering so acutely from rheumatism that for months he had walked with great difficulty, besides which he was suffering severely and was almost incapacitated from his work. With the removal of these teeth, his symptoms were completely relieved and have not returned for five years. He states that he would not have them back for a million dollars. (Incidentally,

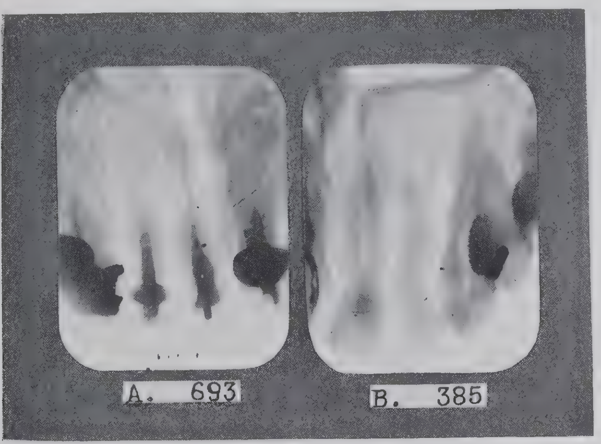

FIGURE 114. INFECTED TEETH WITH NO HISTORY OF DISCOMFORT.

it is of interest to note that the patient reported that his former dentist, following the regulation basis of interpretation, insisted that these teeth could not be related to his condition without showing more evidence of involvement. He also stated that he would eat his own hat if the man were any better after their removal. I have not learned whether he has yet done so but the patient insists that this is his treat.) The significant thing about this patient's teeth in connection with this present study is that they never were in the slightest tender and he had no suggestion or indication of an abnormality or infection.

Figure 114-B shows the teeth of a young lady suffering very severely from rheumatism and heart involvement with no local symptom of tenderness about these teeth, but which were infected, and after their removal with some others her symptoms so completely disappeared that she was able again to work, which she had not been able to do for many months, and in five years has had no recurrence. These two patients belong to the group of strongly inherited susceptibility. On the basis of comfort there was no suggestion whatever that these teeth were not in perfectly safe condition, notwithstanding the lateral contained a putrescent pulp of long standing.

These three groups of illustrations cannot be considered as proving anything since they represent such a few cases. However, they are selected simply as typical of large groups, and, therefore, are significant as typical illustrations. Those in Figure 112 are all classed in the non-susceptible group; those in Figure 113, the acquired group; and those in Figure 114, the strongly inherited group.

SUMMARY AND CONCLUSIONS.

An analysis of these four groups of studies suggests to us the following: That there is a direct relationship between the extent of rarefaction or absorption about roots and the condition of comfort; that this condition of absorption is directly related to the recurring acute inflammatory processes; and conversely, that the absence of extensive areas of absorption accompanies cases without a history of recurring acute processes, and that these two conditions are not directly related in the order of the extent of the absorption to the condition of systemic involvement, but inversely so; for with a given infection, the patients, with a large area of absorption and a history of recurring tenderness of the tooth, have been free from systemic involvements; and those with relatively small areas of absorption in proportion to the capacity of the tooth for infection, have proven to be the patients with systemic involvement. We shall give our interpretation of these phenomena in Chapters 45 to 56.

We would, therefore, reverse the accepted fundamental that comfort and serviceability are criteria of the success of an operation or the dangerousness of a tooth to the safety of a patient to the following:

> **Local comfort not only is not a certain index of success or safety but constitutes both what is probably the greatest paradox and the costliest mistake through loss of health and life that exists in both dental and medical practice, because it may only mean the absence of local reaction which would, if present, incidentally make the tooth sore and fundamentally destroy the infection at its source; whereas, the absence of this local reaction and its consequent destruction of the infection products permits them to pass throughout the body to irritate and break down that patient's most susceptible tissue, which tissue can be anticipated very frequently.**

CHAPTER XVII.

QUANTITY, SYSTEMIC EFFECT, AND TOOTH CAPACITY.

PROBLEM: What is the relationship of the quantity of dental infection to the type and extent of systemic involvement?

EXPERIMENTAL AND DISCUSSION.

That the problem of systemic involvement is essentially the problem of the overwhelming of the natural defenses by a large quantity of dental infection, is a fundamental that seems to be quite universal in its general acceptance. While it is recognized that there is a great difference in the virulence of organisms from various sources, since the capacity of a tooth is so small it is not deemed possible that a properly root-filled tooth will have capacity enough for sufficient dental infection to overwhelm the patient; and furthermore, the organisms constituting dental infections have been reported by so many writers to be of so low virulence, that the professional mind has come to accept that a fundamental requisite for a tooth to be a source of serious involvement will be that there is present, in addition to the infection in the tooth, a quantity of infection in what is considered an abscess or pus sac at the root apex, and which, because of its capacity, comes to be a menace and possible danger. Howe states in his article "The Focal Theory of Infection in its Application to the Teeth"[9] the following:

"In the experimental work that is used to support this theory, young animals, intravenous injections, and massive doses are used. It is replied to the criticisms that these doses are excessive and do not fairly represent what occurs in the human body, that, at times, it is possible to produce the desired pathological effect with smaller doses. These doses range from what in the case of man of 70 kilos. or 154 lbs. would be from ten quarts to a cupful. What is termed a small dose is one or two cupfuls of microörganisms in the case of a man of 154 lbs. Pure cultures are not injected. The granuloma, the abscess, or pyorrheal pus, and the pulp are dropped bodily into ascetic-dextrose broth, allowed to grow, and the broth containing the conglomerate mixture of bacteria, altered and decomposing tissue and its morbid products are injected en masse into animals. . . . . . Now we do not often deal with doses ranging from a cupful to five or six quarts from dental sources. Yet, to produce such results as are described, they must be used. In the small dose of a cupful of microörganisms, together with the other putrefactive products mentioned, possibly or occasionally an effect is obtained. . . . . Others have inoculated rabbits with ten to fifteen c.c. doses of streptococci of this type for three months and nothing has happened."

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[9] See bibliography.

These researches have been conducted to ascertain what the quantity of dental infection may be in various cases, and how much of it may be sufficient to produce systemic involvement, and what may be the capacity of a tooth even with a good root filling as a reservoir or bacterial and toxin generator. Our first problem has been to determine the capacity of the tooth. To do this, we have taken freshly extracted, root-filled teeth, removed all excess moisture, and weighed them. We have extracted the moisture by placing them in a chamber in which the moisture of the air was being extracted by such chemicals as sulphuric acid, none of which came in contact with the tooth. The teeth were again weighed, re-soaked in water, weighed, and again re-dehydrated without carrying the dehydration to the point of removing water of crystallization. Figure 115 shows a group of such teeth; and it is found, in general, that approximately 5% of the volume of every root-filled tooth is a fluid which may be a culture medium and may be abundantly saturated with bacteria.

CHANGE IN WEIGHT OF TOOTH STRUCTURE

Fresh Tooth	Dehydration		$CaCl^2$	H^2O	Net Gain %	Net Loss %
	Weight Before	Weight After	M 0.00706			
No. I	0.9940	0.8910	0.9188		3.02%	
	0.6124	0.5801		0.5770		1.56
No. II	1.0372	0.9280	0.9280		1.33	
	0.8635	0.7500		0.7424		1.01

FIGURE 115.

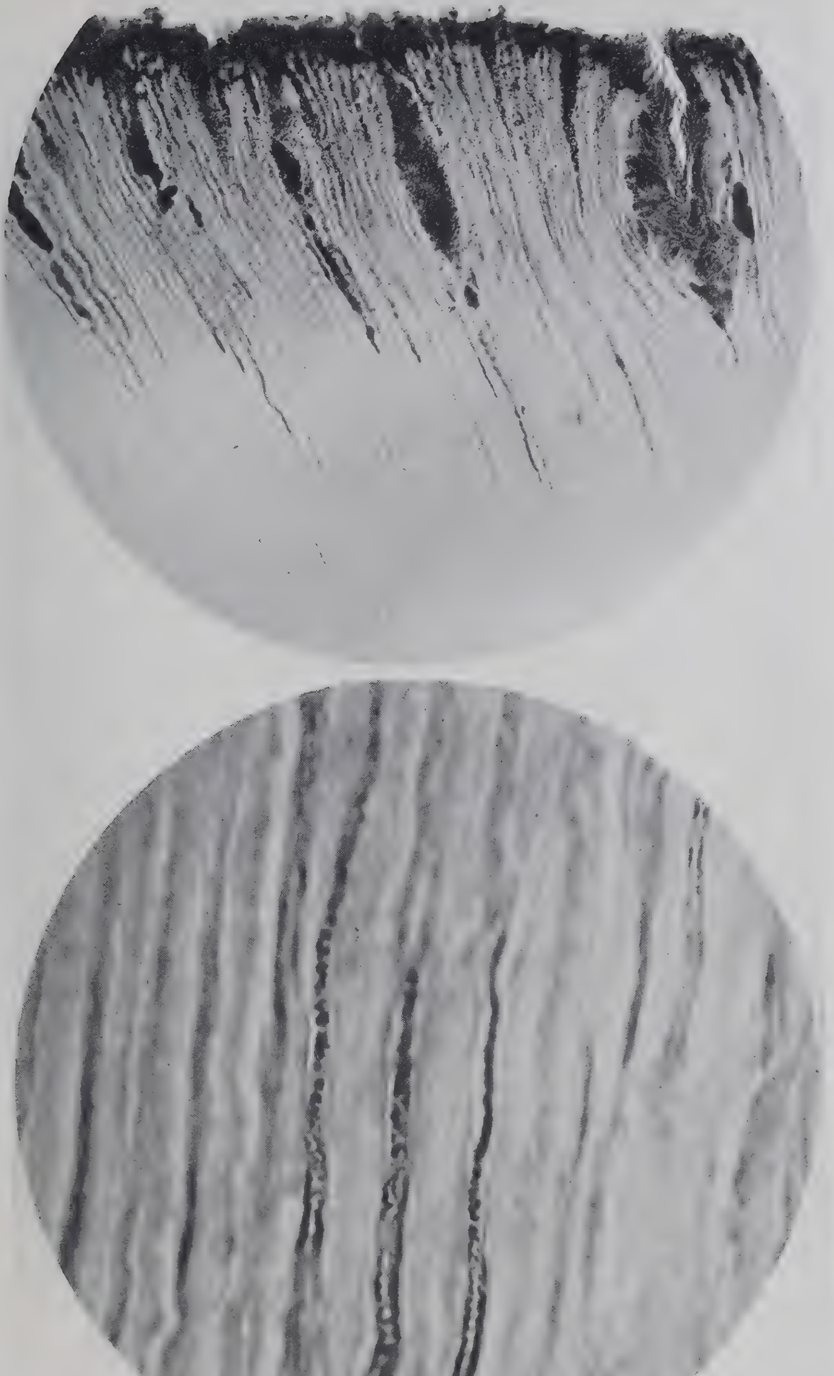

Figure 116. Dental caries extending along the tubuli toward the pulp. Upper is cavity end of tubuli, lower near pulp.

Figure 116 shows the organisms stained directly in the tubuli of the teeth. Many of the earliest efforts to stain bacteria within dental tubuli were confused by the photographing of the abrasive in the tubuli, which, with modern methods of staining, can be readily differentiated from bacteria; and besides, the tissue in Figure 116 was not ground but was decalcified, and there was no opportunity for foreign substances to contaminate the tissue.

The capacity of the pulp chamber for infection may be more or less than that of the total of the dentinal tubuli and acini and canaliculi of the cementum. However, with a large and open root apex, the content of the pulp chamber can be emptied into the tissue without destruction of a large area, and hence with greater concentration than from the dentin. In the construction of the tooth with the laying down of dentin and cementum in juxtaposition, there is established what is, in general effect, a fire-wall between these two structures, which, while it has many small openings uniting these two and a few larger ones, as multiple foramina and accessory canals, impedes the passage from the dentin to the patient of the infection and toxic substances in large amounts.

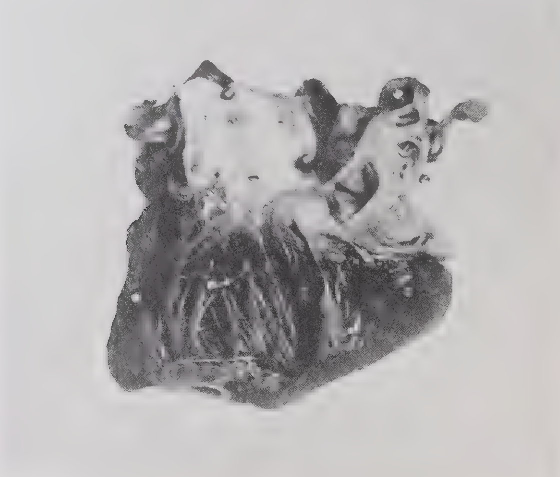

FIGURE 117. ACUTE ENDOCARDITIS, WITH EXTENSIVE VEGETATION ON VALVE CUSP, PRODUCED IN A RABBIT'S HEART BY THE INTRAVENOUS INJECTION OF THE ORGANISMS WASHED FROM A SINGLE ROOT-FILLED TOOTH. THESE ORGANISMS WEIGHED APPROXIMATELY ONE MILLIONTH PART OF A GRAM.

Another phase of this study has included the injection into experimental animals of the organisms that could be washed from a single root-filled tooth. Figure 117 is typical. It shows the heart of a rabbit which has developed acute endocarditis from the injection into the rabbit of the settled washings of the crushings of the tooth of a patient suffering from acute endocarditis. The weight of the organisms injected into this rabbit was determined by counting the number present in a known dilution and, by calculation, establishing the total number approximately, which was found to be a millionth part of a gram.

To answer the question whether there are possibilities of other substances than organisms having been taken from the teeth which produced these disturbances, we have made a large series of studies to ascertain whether toxic substances other than organisms are present in teeth. This we will study in the next chapter. We have also centrifuged the organisms, removed the fluid, and resuspended them in normal salt solution and inoculated them into rabbits, and have produced lesions and death of animals.

An analysis of several hundred individuals from whom teeth were removed having root fillings without evidence of periapical chambers containing infected granulomata, discloses that in a large number there has been a very marked, if not complete, relief of the systemic expression upon the removal of the tooth in question.

To determine whether or not a quantity of infection must be injected into a rabbit which would be equivalent to a "tea-cupful or several quarts per man" I made the following experiment: Into many dozens of rabbits we have planted beneath the skin a freshly extracted tooth to determine what the effect would be of the small amount of infection that a single tooth could contain. These have revealed a very great difference in the virulence of different strains and the type of reaction they would produce. In the chapter on kidney involvements we show several cases in which the planted tooth produced nephritis in the rabbit without the development of an extensive abscess about the implanted tooth, and in some cases the same tooth transferred to another rabbit again produced kidney involvements. In many cases the teeth become incysted. Many of these are discussed in subsequent chapters. Still others produce wasting diseases and the rabbit slowly fails in weight and finally dies. Others produce most violent toxic and bacterial reactions, causing the death of the rabbits in from a few days to a few weeks.

Figure 118 shows a roentgenogram and photograph of a tooth extracted from a patient suffering from a severe systemic involvement of the central nervous system, not suspected to be related to her teeth. This is discussed in further detail in Chapter 66.

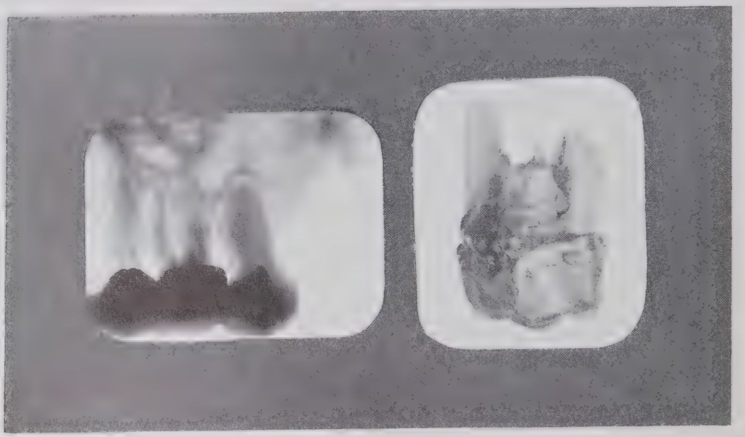

FIGURE 118. TWO VIEWS OF A MOLAR TOOTH PRODUCING NO LOCAL DISCOMFORT FOR THE PATIENT BUT WHICH KILLED MANY RABBITS IN SUCCESSION, IN AN AVERAGE OF FOUR DAYS.

This tooth was placed under the skins of thirty-one different rabbits, twenty-nine of which died spontaneously in from one and one-half to ten days, an average of four days. One of the rabbits which lived ten days, received special treatment to increase its defense. These all died in general of the same symptoms. Another rabbit (Rabbit 986) of this series was injected intravenously with 0.03 cc. of the fluid surrounding the tooth in one of the rabbits. This rabbit was dead in about one and one-half minutes. Another (Rabbit 989) was injected with the highly centrifuged material, which would not be entirely bacteria-free but nearly so, and it was dead in about seven hours. Another (Rabbit 991) was injected intradurally with the bacteria-free filtrate of this material and it died within twenty-one hours. The symptoms and reactions in the animals are discussed in the chapter on diseases of the nervous system, Chapter No. 66.

In order further to study the relation of quantity, very small glass tubes, approximately the size of a fine cambric needle and three-quarters of an inch long, were filled with this material. These open end tubes were placed inside the needle of a hypodermic needle and passed under the skin of a rabbit; and as the needle was withdrawn, the tubes were placed beneath the skin. The quantity of the culture fluid that these needles contained was approximately one five-hundredth of a gram each. From one to four of these small tubes were placed beneath the skins of rabbits and several were used for different types of tests. When placed in the peritoneum, Rabbit 1010 lost 585 grams, or 40 per cent of its weight. It died in 54 days with extreme muscle atrophy.

When placed subcutaneously, Rabbit 1011 lost 460 grams, or 33 per cent, in 38 days. It died of lobar pneumonia, with congestion of the myocardium. Another (Rabbit 1012) with a single tube placed beneath the skin, died in 5 days, with a loss of 75 grams, or 7 per cent, with a very large subcutaneous abscess, and hyperemia of the chest and abdominal viscera.

In order still further to determine this problem, two small round cover slips were sealed together with sodium silicate (liquid silex) and two very small openings left at opposite sides for the organisms to escape. The distance between these cover slips was approximately a fortieth of a millimeter. The area of the plane of fluid was approximately one square centimeter. Hence this quantity was approximately 2.5 milligrams of culture fluid. This exceedingly minute quantity of infection was sufficient to kill this rabbit in 44 days. (Rabbit 995).

A further study of this tooth was made to ascertain the relationship between the size and number of external openings to the danger, as evidenced by the length of time required for the tooth to kill a rabbit after it was planted beneath the skin. It was found, in general, that increasing the number of exits from the dentin increased the toxicity of the tooth apparently by giving a freer exit to the toxic substances. In this connection I think I should state a warning because the need of it has already been evidenced. Immature thinking or experience may suggest that the transferring of the tooth from one rabbit to another is synonymous and comparable with the animal passage of organisms injected intravenously or subcutaneously in lethal amounts, the result of which is to increase the virulence of the organism as it is successively killing the host. In that instance all organisms injected in subsequent animals are direct descendants of those that have lived in the environment of the animal with a lowered resistance, which animal has furnished the entire culture medium for the organisms, and which, because of the quality of adaptation expressed in Chapter 2, induces the organism to increase its aggressive factors. When, however, a tooth is planted beneath the skin of a rabbit and kills the rabbit in two days, and the tooth is then washed and placed under the skin of another rabbit, the organisms in the tooth which are planted in the second rabbit, did not grow in the free body fluids of the dying animal but in the incased moisture within the approximately three miles of closed channels constituting chiefly the dentin, and these organisms have been slightly, if at all, influenced by the presence of the tooth beneath the skin of the rabbit, and practically none of which are the descendants of those causing the death of the animal, or at least producing the infection within the animal's body. The passage of a tooth, therefore, from animal to animal is little more than changing its incubator and does not constitute animal passage in the sense that intravenous injection of a culture is understood.

I have, therefore, conducted experiments to obtain data, if possible, that would indicate whether it is possible for especially vigorous and healthy animals to destroy the virulence of the organisms within an infected tooth. There seems no indication that even the most vigorous animals have been able to render a tooth harmless which had been demonstrated to be capable of producing the death of an animal; and while an infected tooth when placed beneath the skin of a rabbit, kills small animals in proportionally less time than large ones, we have not been able to find a rabbit big enough to withstand the toxic substance of certain infected teeth. I have discussed elsewhere the circumstance of placing such a tooth under the skin of a very large and exceedingly vigorous buck rabbit, that was a most vicious fighter, seriously wounding and killing any other male rabbits he could reach. On placing such a tooth beneath his skin, in a few hours he was sulking in a corner of his cage, and was dead in five days.

This seems clearly to demonstrate that there is a direct relationship between the accessibility of the rabbit or host to the organisms confined within the tooth structure, for it seems very clear that the dentino-cemental junction seems a very considerable barrier. To determine this we have made the following experiment:

Various chemicals and infected culture media have been sealed in the pulp chambers of teeth to ascertain the nature of the substances that were capable of penetrating different structures and parts of the tooth. As discussed in the previous chapter, when a culture of acid producing bacteria is placed in the pulp chamber of a tooth, and the tooth planted in a jellied culture medium, carrying a disclosing die, the presence of the organisms can be read directly by the color change in the surrounding medium. These showed that the organisms leave the tooth only at foramina. When, however, chemicals are used containing electrolytes which are capable of passing through semipermeable membranes, these may pass through the dentin and cementum, or at least appear on all surfaces of the cementum as well as the foramina. This was also demonstrated by sealing the apex.

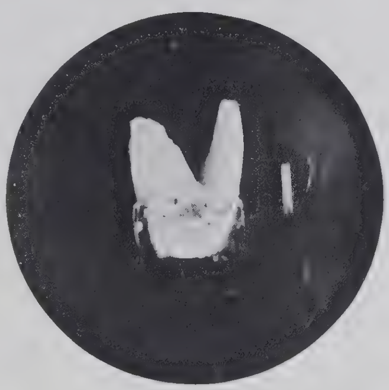

FIGURE 119. SHOWS A SMALL GLASS TUBE CARRYING CHIPS FROM AN INFECTED TOOTH. ITS SIZE CAN BE JUDGED BY COMPARISON WITH THE TOOTH.

One of these glass tubes containing approximately one milligram of the drillings of this tooth is shown beside the tooth in Figure 119; and one of the tubes which was planted beneath the rabbit's skin and open at both ends, containing some of the culture media from the organism growing in this tooth had about the same capacity, being longer but smaller in diameter.

When we compute the actual weight of the organisms, not dry but moist, which were actually found to be capable of killing some of these rabbits, we find it to be approximately one five-hundred-thousandth part of a gram. If we allow that a man is twenty times as large as a rabbit, which is the usual computation, we have a quantity which might be expected to be injurious to man, if not seriously so, of one twenty-five-thousandth part of a gram. Or when we compute the quantity of this culture medium which produced death in these rabbits, approximately one-thousandth part of a gram to kill a rabbit in one and one-half days, and extending it twenty times that might be expected to be mildly or seriously injurious to a man, we find this quantity to be: namely, 20 cubic millimeters (20 milligrams). This figure does not check very closely with Dr. Howe's findings, since a tea-cupful contains about 250 grams or 250,000 milligrams. In other words, the dose that we have found to be sufficient to kill a rabbit is about 1/250,000th part of the minimum amount Dr. Howe has suggested and 1/12,500th part of the minimum amount he has computed to be necessary to injure a person, using his minimum quantity of one tea-cupful instead of his maximum, which he states to be several quarts. As we have stated above, and as we show

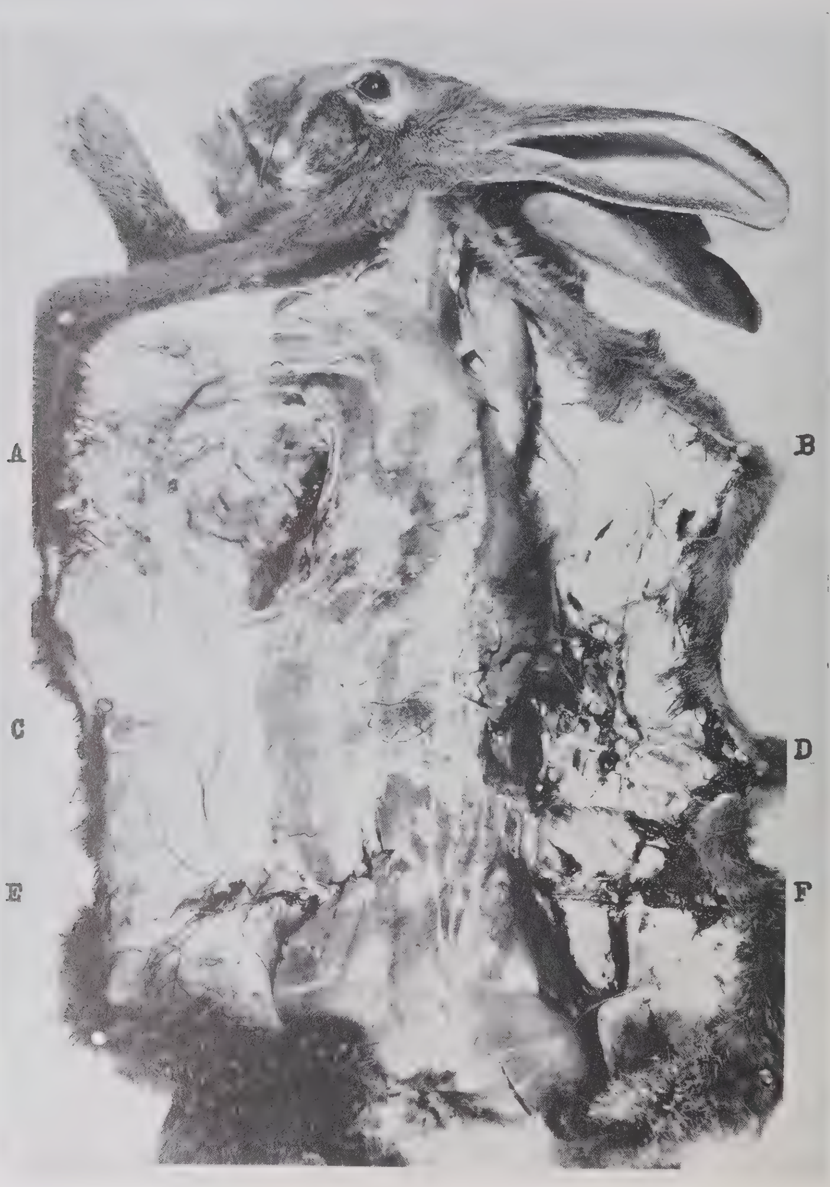

FIGURE 120. RABBIT REACTIONS TO OPEN END TUBES CARRYING DIFFERENT SUBSTANCES. A, VIRULENT CULTURE; B, SAME ORGANISMS WITH TWO PER CENT PHENOL; C, NORMAL SALT SOLUTION; D, ANOTHER DENTAL CULTURE; E, FILTRATE FROM CULTURE A; F, SUPERNATANT FLUID FROM CENTRIFUGED A.

in other chapters, many of the teeth that are planted beneath the skins of rabbits, produce very little disturbance, while others produce very violent disturbance locally and systemically; and still others apparently produce very little disturbance locally where planted, but systemically develop nephritis and heart involvements, as abundantly illustrated elsewhere.

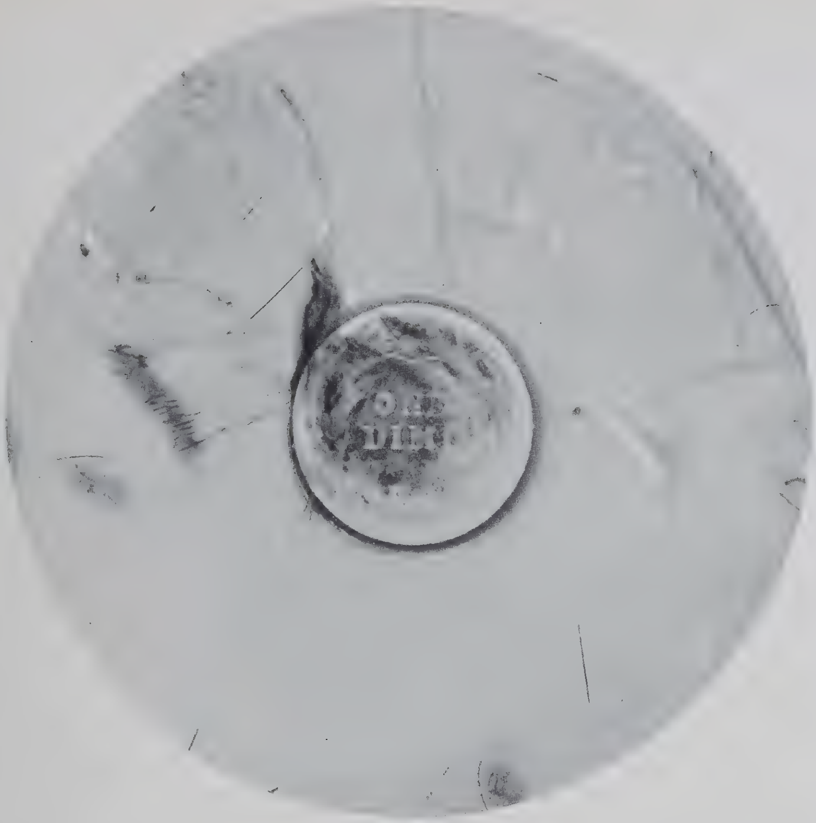

FIGURE 121. APPEARANCE OF A STERILE COIN TWO MONTHS AFTER IMPLANTING BENEATH A RABBIT'S SKIN. NO FIBROUS CAPSULE FORMATION OR IRRITATION. A SLIGHT ETCHING OF THE COIN.

It doubtless will be argued that these teeth planted under the skin of a rabbit, or the glass tubes or any foreign substance, would act as a serious irritant and produce local disturbance if not suppuration. To determine this, at the same time as the tubes shown in Figure 120 showing the abscess produced by the presence of the tube of this culture, similar tubes were planted beneath the skin on other parts of the back of this same rabbit. The large abscess referred to above is shown at A. At B were planted the same organisms but carrying a small quantity of phenol, approximately two per cent; at C, similar tubes filled with normal salt solution; at D, a similar quantity of the organisms grown from a tooth of another patient; at E, tubes containing filtrate of the same culture of A; at F, the supernatant fluid from the highly centrifuged culture used in A. Serious disturbance was produced in the rabbit by only the culture shown at A. (Figure 120).

As a further test of the result of a foreign irritant, and particularly that we might study the difference in the structure of the tissue which would be organizing about a sterile foreign substance and an infected tooth, we planted sterile coins beneath the skin of a rabbit and have sectioned the membranes that have developed. These are considered in the chapter on the structure of granulomata, (Chapter No. 38); and, incidentally, those experiments reveal that even after two months' time a sterile dime, placed beneath the skin, has so little tissue organized about it, that, except that there is no sign of the skin lesion through which the dime was planted, it would seem as though it were planted there but a day or two ago, for the inscription on the metal can very readily be read through the thickness of this tissue, which is an exceedingly thin transparent veil. This is particularly instructive since there has been sufficient local reaction to etch the surface of the dime and quite largely remove the inscription and lettering. This is shown in Figure 121.

RABBITS WITH SUBDERMAL IMPLANTATIONS

Implantations	No. In Group	Spontaneous Death		Chloroform		Still Living	
		No.	%	No.	%	No.	%
Subdermal implantations	237	181	77	30	12	26	11
Total implantations of teeth	209	165	79	26	13	18	8
Sterile coins	6	No loc	al reac	tions			
Capillary tubes	13	7	53	2	15	4	32
Other substances	9	5	56	0	0	4	44
Maximum No. of implantations of teeth from 1 patient	60	58	97	2	3	0	0
Maximum No. of implantations of a single tooth	35	33	94	2	6	0	0

FIGURE 122.

In order further to test the relation of quantity of infection and systemic reaction, it has been desirable to check against the infected teeth, the general effect of foreign substances, sterile and otherwise. Accordingly, a number of substances have been tested. In Figure 122 we show a group of rabbits with subdermal implantations of various kinds. In the group there were two hundred thirty-seven rabbits, two hundred nine of which had teeth of various types implanted beneath the skin. Of this number one hundred sixty-five or 79 per cent, are dead at the time of this writing, having died spontaneously, and twenty-six or 13 per cent, have been chloroformed; eighteen, or 8 per cent are still living. Most of these teeth had been root-filled and were comfortable, so far as the patient was concerned, when they were extracted. Some were normal in health and structure, but malposed, such as third molars; some of these, as noted elsewhere, were removed impactions. Others were treated in various ways such as boiling, sterilizing with medicaments, etc. Even impacted teeth are not necessarily sterile though they probably generally are. In six cases sterile coins were used. In these there was no local reaction. Thirteen capillary tubes containing infected material were implanted, of which seven rabbits, or 53 per cent, died spontaneously. Miscellaneous substances were used in nine rabbits. In this chart, it will be noted that in order to compare the virulence of different teeth taken from the same patient, six different teeth were successively implanted in sixty rabbits. Fifty-eight, or 97 per cent, died spontaneously, and two, or 3 per cent, were chloroformed. The maximum number of implantations made with a single tooth was thirty-five of which thirty-three rabbits, or 94 per cent, died spontaneously, and two rabbits, or 6 per cent, were chloroformed.

It will naturally be argued that experiments made on animals may have little significance in interpreting human defense. In the chapter on bactericidal properties of the blood I have shown the relative defense of various animals, as compared to the human, for streptococcal infection as determined by the methods used; and it is important that few humans have as high a defense for the type of dental organism taken from infected teeth as do the rabbits. Rats and mice have a still higher defense.

SUMMARY AND CONCLUSIONS.

An analysis of these data suggests that pulpless teeth, whether root-filled or not, may, if the dental tubuli are not filled, be reservoirs of culture media, not only constituting approximately one-fifth of the total volume and weight of the tooth, but that this quantity is ample to produce very marked systemic disturbance; that the quantity of infection in such a tooth is sufficient to produce definite lesions in animals and even to produce their death. The clinical reaction by the removal of the systemic symptoms suggests that the quantity of infection was also enough, seriously to affect the patient.

We are, therefore, compelled to change the accepted fundamental that *infected teeth cannot, if the pulp chamber is properly filled, contain infection sufficient seriously to affect the patient,* to the following:

> **Since approximately 5% of every root-filled tooth is a fluid that can become toxic substance or culture media, and in single rooted teeth usually amounts**

to about fifty milligrams, which space may be occupied by organisms which have access to it from either the blood or lymph stream or an exposed surface of dentin, and since death from typical heart lesions has been produced in animals inoculated with the relatively small quantity of bacteria, washed from a crushed tooth, taken from a patient suffering from acute heart involvement, constituting an amount of organisms which, by weight, is approximately a millionth part of a gram, and since the bacteria-free toxin washed from crushed teeth frequently produces very extreme systemic changes, I believe a single rooted tooth with a well filled pulp canal can, under certain conditions, be a source of systemic disturbance. I am also led to this conclusion by our clinical experience with patients.

When infected teeth produce disturbance in other parts of the body, it is not necessary that the quantity of infection be large, nor is it demonstrated that it is necessary that organisms pass throughout the body or to the special tissues involved, but the evidence at hand strongly suggests that soluble poisons may pass from the infected teeth to the lymph or blood circulation, or both, and produce systemic disturbance entirely out of proportion to the quantity of poison involved. The evidence indicates that this toxic substance may under certain circumstances sensitize the body or special tissues so that very small quantities of the organisms, which produce that toxin, may produce very marked reactions and disturbances.

CHAPTER XVIII.

STUDIES OF PULPLESS TEETH, WITH AND WITHOUT ROOT FILLINGS.

PROBLEM: Have pulpless teeth injurious contents other than microörganisms?

EXPERIMENTAL AND DISCUSSION.

A search of the literature has failed to reveal any new light on this question. We find no evidence that teeth contain other injurious substances than bacteria; nor do we find evidence that such a research has been made. A large number of studies has been made of the organisms which develop in infected teeth, both as regards their identity and their biologic and pathologic qualities. The general procedure has been to take the organisms from the suspected teeth by any one of several procedures, culture them in suitable media, and test their reactions on various sugars and on animals as well as determine their morphologic characteristics. In this way, a few organisms are increased into a large number, presumably of their kind, with the effect that the studies are made with new generations grown in new media in a new environment; and if many strains are present, those that can best adapt themselves to the new medium environment, will necessarily develop most rapidly and largely overgrow the less adaptable types.

One of our earliest studies in this connection has been the injection into animals of the washings from freshly extracted and finely crushed, individual teeth. Figure 123 is typical. It shows two rabbits, full brothers, weighing within a few grams of each other, kept continually under the same environment since birth and fed on the same nourishment. A was inoculated with the washing from the crushings of a tooth, which was centrifuged sufficiently to throw down all sediment. A few organisms that were washed from the teeth were left in suspension, but only the clear supernatant fluid was used. B is the control. It gained in weight continually, whereas A began to lose weight slowly. The amount of wash injected was 1 cc. of apparently clear water. In a few days A showed a loss in weight though there was no apparent loss of appetite. Both ate heartily and exercised freely in a roomy

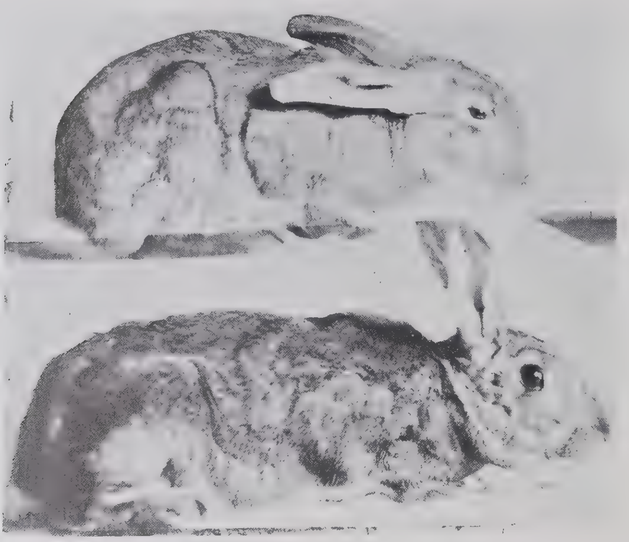

FIGURE 123. TWO BROTHER RABBITS OF CORRESPONDING SIZE AND WEIGHT. ALWAYS UNDER SAME ENVIRONMENT. A, THE UPPER, WAS INJECTED INTRAVENOUSLY WITH 1 CC. OF THE CLEAR CENTRIFUGED WASHINGS OF AN INFECTED TOOTH; B, A CONTROL. A LOST 37% AND DIED IN FIVE WEEKS AND B GAINED 12%.

cage. Week after week A was losing in weight and B was gaining in weight. At the end of four weeks, A had lost about 25 per cent in weight; B had gained about 10 per cent in weight. At the end of five weeks, A died, having lost about 37 per cent, in which time B had gained about 12 per cent. On post, A showed a general marasmus with marked atrophy of all muscle tissue, and development of changes in the digestive tract.

In Chapter 2, I have discussed the morphology and biological characteristics of the organisms involved in dental infections. In general, we have found that their most important characteristic is their power of adaptability. In Figure 24 of that chapter it was revealed in the spontaneous deaths the organisms, that were washed free from the culture medium and injected into animals, killed in an average of seven days, with a loss of weight of 2 per cent per day; whereas, when the whole culture was injected, they died on an average of six days, with an average loss of 3 per cent per day. This suggested that there was some toxic factor present in the culture medium that was injurious and was additive to the injury of the organisms.

Our problem in this chapter is to determine somewhat of the general nature of these toxic products. To ascertain this, seventeen rabbits were injected with the filtered washings from infected teeth, and it should be noted that this was not the washing of a quantity of bacterial growth but simply the accumulated toxic substance present in a single tooth in each case. Of these seventeen rabbits, thirteen died spontaneously in an average of five days, with a loss in weight per day of 3.8 per cent. Inasmuch as the organisms which produced the toxin in these particular teeth were not the same strains of organisms represented in the chart in Figure 24 of Chapter 2, we cannot, by this comparison, compare the organisms with their identical toxins. However, since the organisms in all these cases are diplococci and streptococci, they are, in general, comparable.

Another most striking result of this experiment was that of fourteen rabbits injected with the unfiltered washings, in which the toxic substance plus what bacteria would wash from the crushed tooth would be involved, eight died in an average of twelve days, with a loss in weight per day of 1.8 grams. We are at a loss to understand why, in these cases, the toxic substance alone washed from the tooth is more rapidly fatal than the toxic substance plus the organism, unless it be that it is the presence in the blood stream or body fluids of the dead or living organisms which furnish the necessary activity to call forth the antitoxins to combat this toxic factor. I am inclined to believe that this is the explanation. In this chart in Figure 124, it is interesting to note that only four of seventeen rabbits lived more than a few days, thirteen dying in an average of five days. One of the rabbits of

COMPARISON OF FILTERED AND UNFILTERED WASHINGS

Filtered Washings								
No. in Group	Death	Days Lived	Loss			Gain		
			Actual	%	% per day	Actual	%	% per day
3	Chloroformed	33	56	5	.1			
1	Chloroformed	44				176	18	.4
13	Spontaneous	5	191	19	3.8			
Unfiltered Washings								
5	Chloroformed	32				171	14	.4
1	Chloroformed	20	191	10	.5			
8	Spontaneous	12	221	22	1.8			

FIGURE 124.

this group received a washing which, apparently, was not at all toxic, or but slightly, for it gained 18 per cent in forty-four days; and, similarly, five of the group of fourteen that received the unfiltered washings, gained an average of 14 per cent; whereas, all the others in each group lost in weight. In the chapter on Sensitization, I have discussed the matter of the ability of these toxic substances to sensitize tissues of the host so that when later injected with the toxic substance or when the organisms producing it are injected into the host, the reactions are much more violent than otherwise. One rabbit died within a few minutes.

These data suggested to us that we are dealing with products in freshly extracted, infected teeth, which differ essentially from those developed by culturing the organisms from the same. We, accordingly, made determinations of the difference in the reactions when the organisms were removed from the washings, and found that in many instances that after passing the washings of the crushed tooth through a fine Berkefeld filter very similar disturbances were produced in animals even though the cultured filtrate developed no organisms. It was found that, whereas the organisms, when injected, tended definitely and regularly to produce lesions in various organs and tissues, the filtrate produced disturbances of metabolism and nutrition, with its principal effects upon the digestive tract and nervous system. It is evident that we are dealing in infected teeth with a substance which has very profound effect in very small quantities. The substance is a very complicated one which does not lend itself readily to concentration, as will be shown later.

We have next inoculated succeeding groups of animals with the filtered washings from teeth, and then tested these animals to determine whether they were more sensitive to the organisms grown from those teeth than our normal animals; and it has been found that whereas the controls—namely, the animals that had not received a preliminary injection of the filtrate—developed lesions in one or two weeks and usually recovered according to the sizes of the doses used in the tests, the animals that were inoculated with the filtrate usually developed their symptoms much more rapidly and severely. A much larger percentage died and often within a day or two; and in a few instances, the preliminary injection of the filtrate so prepared the animal for the bacterial injection that it died within thirty minutes to two hours, and in one instance in a few minutes; whereas the controls lived for weeks and often apparently recovered entirely. We believe this is one of the most important of the many new discoveries of our work. Its interpretation and significance are given in Chapters 45 to 56.

SUMMARY AND CONCLUSIONS.

We are, therefore, led from these studies to conclude:

> **That the organisms found in infected teeth are not the only product of that tooth which may disturb the host, that toxic substances are formed in the tooth which may pass from that tooth to the host, and in some instances (perhaps in many) tend to prepare the host for the invasion by that organism, and may, either in addition or separately from that process, produce definite disturbances of metabolism within the host.**

We would, accordingly, change the old fundamental: namely, that *the only injurious substance which infected teeth may contain is a bacterium;* or *infected teeth contain no other injurious substances than microörganisms,* to:

> **Infected teeth may contain in addition to microörganisms toxic substances, which produce very profound effects upon experimental animals and, which tend to prepare the tissues of the host, at least in some cases, for a more ready invasion by the organisms growing in that tooth.**

CHAPTER XIX.

HEMATOLOGICAL CHANGES IN THE BLOOD.

PROBLEM: What changes are produced in the blood and sera of the body by dental infections?

EXPERIMENTAL AND DISCUSSION.

While it has been known for a long time that many patients suffering from rheumatic group lesions, which have affected various of the harder tissues, such as the muscles and skeleton, nervous system, circulation, digestive tract, etc., there seems to have been very little work done to determine the effect of dental infections upon the various sera of the body. An analysis of over one thousand blood counts of animals discloses, that, whereas a given strain of organisms tends to produce, in general, the same changes in the blood picture, different strains may produce widely different results.

Figure 125 shows a group of rabbits which received their infection by having teeth planted beneath the skin. These were such teeth as were condemned because of suspected systemic involvements of the patients. We have selected for this group a series having from two to three counts and in which there has been an increase in the erythrocytes. It will be noted that in two instances, five are from the same patient.

Similarly, some cultures and implanted teeth tend to produce a decrease in the erythrocytes and, occasionally, very marked decrease. In Figure 126 we have a group of rabbits showing decreases in both the hemoglobin and erythrocytes, which are typical. The first decreased from 6,750,000 to 4,600,000 in twenty-four hours. The hemoglobin decreased 5 per cent, and incidentally, there was a decrease in the leucocytes. These, however, will be discussed in subsequent paragraphs. This rabbit was inoculated with culture. The second had a tooth implanted beneath the skin. The hemoglobin reduced 5 per cent, and the erythrocytes from 6,900,000 to 4,200,000 in eight days. The third shows a quite remarkable picture. This rabbit had a tooth planted beneath the skin; and while its hemoglobin remained constant, the erythrocytes reduced from 4,050,000 to 1,650,000,

ERYTHROCYTOSIS PRODUCED BY TOOTH IMPLANTATIONS

Case No.	Rabbit No.	Date	Erythrocytes
1236	813	2–15–22 2–23–22	3,900,000 4,600,000
1215	820	2–15–22 2–23–22	2,600,000 5,650,000
1215	821	2–15–22 2–19–22	2,056,000 3,050,000
527	822	2–16–22 2–23–22 3–29–22 3–30–22	1,050,000 2,750,000 5,200,000 8,500,000
	824	2–16–22 2–23–22	1,080,000 3,950,000
	825	2–17–22 2–23–22 2–28–22	5,700,000 7,700,000 6,750,000
	826	2–17–22 2–25–22 2–28–22	4,800,000 5,050,000 9,750,000
	851	3– 8–22 3–20–22 4–15–22	1,450,000 2,450,000 6,200,000
334	871	3–17–22 3–20–22 3–24–22 3–28–22 4– 4–22 4–15–22	3,050,000 1,300,000 5,900,000 6,300,000 7,050,000 6,900,000
1396	879	3–20–22 3–27–22	2,600,000 5,000,000
1222	828	2–18–22 2–20–22	3,500,000 4,500,000
1241	882	3–22–22 3–27–22	5,700,000 6,700,000
1241	894	3–22–22 4– 4–22	4,300,000 5,300,000
682	880	3–22–22 3–24–22 4–11–22	1,200,000 5,500,000 6,450,000
	838	2–22–22 3– 2–22	2,750,000 3,750,000
	839	2–22–22 3– 2–22	1,750,000 3,750,000
	840	2–22–22 3– 2–22	2,750,000 4,750,000
	843	2–22–22 2–25–22	2,400,000 3,400,000
1170	827	2–18–22 2–20–22 2–22–22	1,050,000 2,050,000 6,550,000
1205	831	2–20–22 2–22–22	3,080,000 5,050,000

Figure 125.

ERYTHROPENIA

Case No.	Rabbit No.	Hemo-globin	Erythrocytes
1322	960	80 75	6,750,000 4,600,000
1119	1057	85 85 80	6,900,000 5,800,000 4,200,000
692	849	80 80 80	4,050,000 5,050,000 1,650,000
692	868	80 75 75	3,600,000 2,900,000 750,000

Figure 126.

and the color index raised from 0.9 to 2 in twelve days. The fourth rabbit had a decrease in the hemoglobin from 80 to 75; the color index raised from 1 to 4; and the erythrocytes reduced from 3,600,000 to 750,000 in six days.

The most striking changes in blood morphology, however, have been produced in the various types of leucocytes, expressing themselves generally at first by leucocytosis, followed by a leucopenia. A group of these typical changes in leucocyte count is shown in Figure 127. The most striking effect, however, of the effect of the infection on the leucocyte count is expressed as a marked leucopenia, the reduction of leucocytes frequently being very great. This is shown in Figure 128.

LEUCOCYTOSIS PRODUCED BY TOOTH IMPLANTATIONS

Case No	Rabbit No	Leucocytes
1367	1135	9,000 13,000
	1134	8,300 11,400
1370	1154	8,000 11,000 6,100
1390	1158	8,400 17,600
1353	1169	8,800 10,000 8,200
1363	1170	8,200 10,200 9,800 9,300 5,600
1317	1186	5,600 6,900 4,000 2,600
1388	1204	7,900 20,000
1394	1211	8,600 18,000
404	1153	8,200 6,200 10,800
355	1173	10,800 10,200 12,200 23,800
1385	1175	15,300 14,400 25,400

FIGURE 127.

For years I have been noticing a type of blood picture in patients suffering from dental infections, which is characterized by a low polymorphonuclear count and a high small lymphocyte count; and these studies seem to have thrown a new light upon this condition. I had noticed that it often changed, returning to or toward normal in the patients after removal of dental infections. In Figure 129 I show the successive counts of a series of eleven rabbits, each one of which had a tooth implanted beneath the skin. The first reading in each case was made before the

LEUCOPENIA PRODUCED BY TOOTH IMPLANTATIONS

Case No.	Rabbit No.	Leucocytes
1317	1167	11,500 7,200
	1186	5,600 6,900 4,000 2,600
1387	1178	10,800 9,600 5,000 6,000
1377	1208	25,000 7,000

FIGURE 128.

implantation and represents approximately the rabbit's normal. In this series, we have shown in heavier faced type, the polymorphonuclears and small lymphocytes, and it will be noted that in every instance in this group there was progressive depression of the polymorphonuclears, with a corresponding increase in the small lymphocytes. The average percentage decrease of polymorphonuclears is 33 and the average percentage increase of small lymphocytes 58. It is interesting to note that while the very serious changes in the different types of leucocytic cells have occured, there has been very little change in the hemoglobin of these animals, as shown in that column. It is also important to note the slight change that has been produced in the erythrocytes in these cases. In the third and fourth column we have shown the weight changes, total and per cent, and it is important that in those cases with very marked loss in weight (for all of these rabbits lost in weight,) almost in proportion with the loss there has been the depression of the polymorphonuclears and an increase in the lymphocytes. We have here an expression of the phases of blood morphology that are involved in the Walker Index, which we have discussed chiefly in the chapters on systemic involvements in patients, in which cases we have referred occasionally to the negative Walker Index.

An illustration would be shown in Case No. 1228, in which the patient was suffering from acute heart involvement and acute rheumatism with albuminuria, with evidence of direct relationship to focal dental infections. The polymorphonuclear count

EFFECT OF TOOTH IMPLANTATIONS IN DEPRESSING POLYMORPHONUCLEARS AND INCREASING LYMPHOCYTES

Case No.	Rabbit No.	Weight Loss		Hemo-globin		Erythro-cytes	Leuco-cytes	Poly-morpho-nuclears %	Lymphocytes		Eosino-philes %	Baso-philes %	Mono-nuclears %	Color Index
		Actual	%						Small %	Large %				
1317	1055	163	12	B	85	5,500,000	7,000	**55**	**30**	10	1		4	.7
				A	85	6,700,000	8,400	**50**	**37**	7		2	4	.6
				A	80	7,950,000	18,000	**38**	**49**	9		1	3	.5
				A	85	6,050,000	7,000	**44**	**43**	8		2		.7
1119	1057	100	8	B	85	6,900,000	12,200	**39**	**44**	9		3	5	.6
				A	85	5,800,000	12,800	**32**	**52**	8		4	4	.7
1353	1097	211	19	B				**60**	**23**	11		2	4	
				A	80	5,150,000	22,200	**57**	**27**	8	1	2	5	.7
				A	80	4,600,000	8,600	**39**	**51**	8		1	1	.8
1363	1123	114	10	B	85	5,200,000	12,600	**42**	**43**	8		1	6	.8
				A	80	5,600,000	6,800	**40**	**37**	19		1	3	.7
				A	80	4,300,000	7,200	**26**	**58**	14			2	.9
1363	1125	263	17	B	85	5,800,000	10,200	**63**	**22**	10		1	4	.7
				A	80	6,400,000	5,800	**59**	**27**	9		2	3	.6
				A	80	7,200,000	5,800	**43**	**43**	9			5	.5
404	1126	519	30	B	85	7,400,000	15,600	**60**	**29**	8		2	1	.6
				A	80	7,300,000	9,200	**36**	**51**	9			4	.5
				A	80	6,900,000	5,600	**38**	**51**	9		1	1	.6
				A	85	6,800,000	14,300	**34**	**52**	14				.6
1353	1128	440	28	B	85	7,350,000	10,200	**44**	**42**	12		1	2	.6
				A	85	7,100,000	9,600	**46**	**34**	10		6	4	.6
				A	85	6,250,000	15,600	**31**	**49**	14		1	5	.7
1346	1130	440	37	B	85	4,350,000	12,900	**60**	**31**	5		2	2	.9
				A	80	5,050,000	7,800	**29**	**58**	11			2	.7
				A	80	5,250,000	14,800	**39**	**53**	8				.7
1363	1131	354	36	B	85	6,450,000	8,000	**45**	**44**	9			2	.6
				A	80	6,000,000	6,800	**43**	**47**	10				.6
				A	80	6,800,000	5,500	**26**	**61**	13				.6

B. Before implantation
A. After implantation

Average percentage decrease of polymorphonuclears..........33
Average percentage increase of small lymphocytes............ 58

FIGURE 129.

was 83 per cent, which would call for a leucocyte count of at least 23,000 and she only had 10,500. She, accordingly, had a Walker Index of — 12. A blood culture was, accordingly, made, and the same strain of streptococci was found in the patient's blood as was found in the extracted tooth. With the removal of her dental infections, her condition improved very greatly. Her Walker Index reduced to — 4; and, when taken later when the patient was normal, her Walker Index had returned to approximately normal.

PATIENTS WITH DEPRESSED POLYMORPHONUCLEARS AND INCREASED SMALL LYMPHOCYTES

Case No.	Hemo-globin	Erythrocytes	Leucocytes	Polymor-phonu-clears	Lymphocytes		Mono-nuclears	Eosino-philes
					Small	Large		
1381	90%	4,600,000	7,200	**50.0%**	**35.5%**	7.0%	3.5%	1.5%
1267	85%	5,600,000	7,800	**48.5%**	**42.0%**	6.0%	2.0%	0.5%
1311	80%	5,800,000	5,200	**56.3%**	**34.0%**	6.2%	2.6%	0.9%
1405	85%	4,700,000	7,800	**58.3%**	**36.3%**	3.6%	0.8%	0.5%
1403	80%	5,750,000	6,800	**50.0%**	**42.0%**	4.5%	2.5%	
1404	85%	5,300,000	5,600	**56.8%**	**34.1%**	5.4%	2.7%	1.0%
955	85%	5,100,000	9,240	**50.0%**	**40.0%**	8.5%	1.0%	0.5%

FIGURE 130.

In Figure 130 we show a group of consecutive cases, being patients suffering from dental infections of long standing and all showing systemic involvements which I have interpreted to be influenced directly by the dental infections, if not largely produced by them. When we compare these with a case (Case No. 1385) of acute rheumatism which developed suddenly following a chilling of the patient, whose defense was lowered and who at the same time was carrying such chronically infected teeth, we find his blood count as follows:

Hemoglobin	90%
Erythrocytes	5,500,000
Leucocytes	16,000
Polymorphonuclears	78.6%
Small lymphocytes	13.8%
Large lymphocytes	4.1%
Mononuclears	3.0%
Eosinophiles	0.5%
Color Index	0.8

Note that his polymorphonuclears are 78.6; his small lymphocytes, 13.8. It must not be understood that I am presuming that all cases of low polymorphonuclear count have dental infections, nor that all patients with a high lymphocyte count, or both, have thereby an evidence of dental infection. I am submitting for your consideration the fact first that it occurs in the patients with chronic dental infections, and that it develops in our experimental animals in which we produce such states.

SUMMARY AND CONCLUSIONS.

While the data available are not sufficient for detailed deductions, they strongly indicate that there is much significance from both the pathological and diagnostic viewpoints in the blood morphology and its changes. The evidence strongly suggests that the toxic elements involved in the infection process have distinct and harmful effects; and while the reaction to infection of a normal defense is characterized by a leucocytosis (a fact which is quite universally recognized), it seems quite as universally true that certain types of infections, such as those produced by the planting of a tooth beneath the skin of a rabbit, have destructive effects, particularly on the polymorphonuclears, the depression of which decrease in the presence of the increasing infection, spells a very bad omen in the case of our animals, and practically always terminates in death. It, therefore, seems probable that our patients, who show a very marked leucopenia, and particularly with a markedly depressed polymorphonuclear count, are undergoing a degenerative process. Our application of this is discussed in Chapters 45 to 56.

We would, accordingly, condense the conclusions of this chapter to the following:

> **Dental infections may produce very serious changes in the blood and sera of the body, some of the most frequent of which are leucopenia, erythropenia, lymphocytosis, and hemophilia.**

CHAPTER XX.

CHEMICAL CHANGES OF THE BLOOD.

PROBLEM: What are the chemical changes that are produced in the blood by acute and chronic dental focal infections?

EXPERIMENTAL AND DISCUSSION.

The preceding researches led us step by step through clinical expressions of dental infections, local and systemic, through a channel that has led us back into a mountain vastness, uninhabited and unexplored, and quite uncharted. I was led to make this mode of attack as a result of the study of the apparent causes of success and failure in the various lines of research that have been conducted, for apparently exceedingly few solutions to problems have been found by a direct attack on fundamental problems. The symptoms of dental infections are their clinical expressions. By association and exclusion we have been able to type the local structural expressions and also the physical manifestations. These have led directly to changes which occur in the hard structures of the body as increases or decreases in the density of a bone, and in the soft tissues as edema, atrophy, and disfunction. If rarefying osteitis is associated with an entirely different type of defense and reaction from that which obtains when condensing osteitis develops, it would seem most logical that those elements which are directly related to bone formation and tissue function must be most vitally involved. Accordingly, from nearly every research that has been herewith recorded, we have had evidence pointing directly to those factors which are most intimately related to metabolism and bone formation.

As a first approach we have made blood analyses of many hundreds of patients and animals to determine, if possible, what factors are most variable in the different clinical expressions and to what extent. In Figure 131, I show 146 successive blood chemical analyses for 92 successive patients, some individuals having had several determinations made. In these studies we have determined, in general, blood sugar, (Usually the first

COMPARISON OF BLOOD CHEMISTRY, DENTAL PATHOLOGY, AND SYSTEMIC INVOLVEMENTS

Case No.	Sugar	Non-protein Nitrogen	Uric Acid	Urea	Biological Determination				Chemical Determination		Dental Symptoms	Systemic Symptoms
					Calcium Ionic	Calcium Ionic plus Combined	Calcium in Combination	Thrombin	Calcium	Alkalinity Index		
1334	102	28.8				13.20		11.52	12.03		Locked. Rarefying.	Sensitization.
1337	118		4.41 3.12		9.40	11.12 11.84	2.44	14.44 21.60		39.40	Locked. Rarefying.	Neuritis.
1339	107	38.2			7.61 8.07	8.30 8.72	0.69 0.65	10.52 14.13		39.5	Locked. Rarefying.	Neuritis.
1338	109		2.0		12.28	12.52	0.24	7.73			Rarefying. Periodontoclasia.	Ear involvement.
1343					10.86	11.95	1.49	7.14			Locked apical.	Heart.
1342					9.77	11.95	2.18	5.43			Periodontoclasia. Extensive rarefying.	Normal.
812					9.84 10.76	10.76		12.16 9.24			Chronic periodontoclasia.	Lassitude.
410	109				12.47 11.95	12.47 12.03	0.08	11.53 20.05		34.4	Periodontoclasia.	None.
1348	102			7.50	6.84 9.62	7.87 11.42	1.03 1.80	12.16 19.38			Locked apical. Chronic periodontoclasia.	Sensitization.
1346	108	49.0		12.54	9.62	11.31	1.69	20.38			Locked apical. Chronic periodontoclasia.	Neuritis. Heart involvement.
					6.09	7.66	0.57	23.91				
						11.73		10.77				
	83	36.0	3.95	12.07	10.31	12.65	2.34	7.69		47.2		
			3.18		9.38	12.16	2.78	21.62				
	93	37.4	3.34	13.22	10.34	11.60	1.26	16.66		39.2		
	130	27.3	3.87		10.067	10.600	0.533	5.333				
1347	103				11.21	11.52	0.31	22.79			Periodontoclasia.	Sensitization.
735	101				7.67	11.21	3.54	18.33			Locked.	Pregnancy.
1317	98	33.0	2.4		12.87	13.44	0.57	14.13			Locked. Chronic periodontoclasia.	Lassitude. Mild nephritis.
1411	135	31.0	2.7		12.643	13.20	0.557	12.36			Chronic periodontoclasia	Toxemia. Bacteremia

FIGURE 131 (A)

1364	105	24.0	1.8		12.206	13.44	1.234	6.594			Locked apical.	Lassitude.
1365	103	39.0	2.08		11.536	12.34	0.804	7.624			Locked apical.	Neuritis of spine.
1367	119 103 93 90	26.0 46.0 24.0			11.804 11.536 11.402 11.67	14.22 13.66 13.222 13.124	2.416 2.124 1.82 1.454	6.996 6.264 13.598 11.33			Chronic periodontoclasia. Locked apical.	Brain disfunction spasmodic.
1371	105	26.5			11.67	12.33	0.74	5.67			Chronic periodontoclasia.	Skin lesions.
1307	131	26.4			10.667	12.732	2.055	6.133			Chronic periodontoclasia. Locked apical.	Eye involvements Lassitude.
1372	92				10.033	10.804	0.77	7.34			Locked apical.	Neuritis.
1370	102	26.0			10.867	12.47	1.603	10.133			Chronic periodontoclasia. Locked apical.	Lassitude.
1200	106 73	27.0 32.0			9.84	10.333	0.493	7.16			Chronic periodontoclasia. Apical.	Lassitude. Digestive disturbance.
1373	108	28.2	1.36		11.134	12.464	1.330	7.667			Locked apical.	Heart.
1016	62 77	25.6 27.0	1.16		11.670	11.670		10.33			Normal.	Nearly normal.
1374	122	26.2	2.12		8.897	9.680	0.783	8.733			Locked apical.	Underweight. Nerves.
1040	111				12.34	12.34		10.46			Periodontoclasia.	Normal.
1376	94	47.4			11.534	12.866	1.222	3.667			Apical. Periodontoclasia.	Skin sensitization.
1382	82 121 93	25.6 23.6 30.0			10.576 10.801 10.134	12.753 11.402 12.340	2.239 0.601 2.206	12.424 6.399 7.667			Locked apical. Mild periodontoclasia.	Xerostomia.
1381	128 92	33.0 35.0			8.256 10.801	10.55 12.608	2.294 1.807	7.144 12.392			Locked apical.	Lassitude. Rheumatism. Physical symptoms improved.
1383	98.6	28.8			10.267	11.402	1.135	8.733			Locked apical.	Rheumatism.
1385	99	27.6	3.3		9.840	10.801	0.961	13.16			Locked apical.	Acute rheumatism.

FIGURE 131 CONTINUED (B)

COMPARISON OF BLOOD CHEMISTRY, DENTAL PATHOLOGY, AND SYSTEMIC INVOLVEMENTS

Case No.	Sugar	Non-protein Nitrogen	Uric Acid	Urea	Biological Determination				Chemical Determination		Dental Symptoms	Systemic Symptoms
					Calcium Ionic	Calcium Ionic plus Combined	Calcium in Combination	Thrombin	Calcium	Alkalinity Index		
1410	119.3	32.2	3.1		9.44	9.84	0.4	9.56			Normal.	Acute cold.
1262	75				10.23 10.81	11.42 12.03	1.19 1.22	20.77 19.19			Locked apical.	Duodenal ulcer.
1349					9.54	12.05	2.51	8.56			Acute apical abscess.	Fever. Lassitude.
1409	98 93	22.0			12.26 10.04	12.26 11.33	1.29	10.74 3.51		31.8	Locked apical.	Lassitude.
355			2.56		12.27	12.79	0.42	16.73			Normal.	Chronic deforming arthritis, not acute.
1350					9.06	9.66	0.6	10.34			Normal.	Normal.
1353	98 83 88 96	25.0 25.0 24.0	1.44 2.26 2.06 2.72		11.71 11.92 9.25 9.45 10.267	12.82 11.92 13.23 11.61 11.536	1.11 3.70 2.16 1.269	11.29 16.08 15.73 20.00 8.333	10.504		Extensive chronic periodontoclasia.	Nervous breakdown.
987	97	38.0 35.6			9.32 9.61 9.004	10.07 10.53 9.40	0.75 0.92 0.396	17.68 20.39 13.996			Normal.	Multiple recurring rheumatic group lesions.
1120	113 80	29.3 45.0	1.7	13.0	10.67	11.53	0.86	7.33			Normal.	Normal.
1354	96	18.0	1.13		10.58	11.40	0.82	9.42	11.64		Locked apical.	Acute neuritis.
1355	112	28.5			10.77	11.87	1.10	12.23			Apical.	Disturbed vision.
1332	79	27.0			10.39	12.8	2.41	19.11		46.0	Normal.	Normal.
1407	110	28.0			11.13	12.61	1.48	6.87			Mild periodontoclasia.	Normal.
1358	76	18.5	1.16		9.92	9.92		4.08			Normal.	Normal.

FIGURE 131 CONTINUED—C.

1357	142	33.0			12.74	13.22	0.48	5.54			Mild periodontoclasia.	Normal.
1359	98	36.0	2.56		11.06	13.22	2.16	7.54	10.50	41.0	Locked apical.	Hypertension. Nephritis.
1408	115	27.0			11.26	12.48	1.22	13.74	11.733		Locked apical. Periodontoclasia.	Lassitude.
1228	113 102	29.8 34.0	1.55	20.5	11.134	11.938	0.80	15.86	8.29		Locked apical. Normal.	Very acute rheumatism and heart involvement. Normal.
1363	127 116 112	55.0 45.0	3.16		12.598 11.904 12.474	15.04 15.40 13.66	2.442 3.496 1.186	7.96 12.016	9.873	36.14	Apical. Chronic periodontoclasia.	Mild nephritis.
955	113				11.134	13.00	1.866	6.467			Excessive caries.	Xerostomia.
1404	105.6	33.4	3.55		11.802	13.334	1.532	4.998			Chronic periodontoclasia.	Neuritis.
1403	76	20.0	2.98		10.734	11.134	0.40	8.266			Locked apical.	Pelvic surgical.
1311					6.67	9.81	2.14				Nearly normal.	Acute and chronic deforming arthritis.
1325	106 116	35.3			10.50 10.68 9.86	11.25 10.93 10.58	1.20 0.25 0.72				Chronic periodontoclasia.	Lassitude.
1317	96	28.0			7.88 11.13 8.72 8.68	9.43 11.15 9.83 10.18	1.55 0.02 1.11 1.50		10.13		Chronic apical.	Lethargic encephalitis.
1267					7.05	9.47	2.24				Locked apical.	Nervous breakdown.
701					9.36	11.36	2.00				Normal.	Mild rheumatism.
1269					9.66 10.36	11.71 13.65	1.05 3.29				Locked apical.	Syringomyelitis.
1319					8.62	10.05	1.43				Locked apical.	Rheumatism. Heart involvement.

FIGURE 131 CONTINUED—D.

COMPARISON OF BLOOD CHEMISTRY, DENTAL PATHOLOGY, AND SYSTEMIC INVOLVEMENTS

Case No.	Sugar	Non-protein Nitrogen	Uric Acid	Urea	Biological Determination				Chemical Determination		Dental Symptoms	Systemic Symptoms
					Calcium Ionic	Calcium Ionic plus Combined	Calcium in Combination	Thrombin	Calcium	Alkalinity Index		
1321					9.75	11.02	1.27				Locked apical.	Neuritis. Nervous breakdown.
817					9.89	10.13	0.24				Normal.	Normal.
1326					8.42						Locked apical.	Rheumatism.
1312					9.53	10.52	0.99				Extensive apical. Rarefying osteitis.	Lassitude.
1268	295	47.0		15.2	9.33	11.67	2.24		12.32		Chronic periodontoclasia.	Diabetes.
	410	31.0	5.4	16.6					12.18			
1315					5.25 6.37 8.66	7.50 9.02 9.93 10.26	2.25 2.67 1.60				No involvements.	Neuritis of right side.
381					7.99 8.24 6.68	10.75 10.15	2.76 1.91				Locked apical.	Acute rheumatism and arthritis.
1322					8.17 8.39	9.21 9.65	1.04 1.26				Locked apical.	Rheumatism. Heart involvement.
1285	106	42.0	7.54	19.50					8.78		Locked apical.	Neuritis.
1272	116	26.0	4.6	12.0					11.4		Chronic periodontoclasia.	Normal.
1288	102	30.0	5.4						12.1		Chronic periodontoclasia.	Nervous irritability.
1295	96	28.0	3.6						11.54		Dental cyst.	Insomnia.
1406	100	36.9	3.63		11.67	12.205	0.535	13.33			Extensive locked apical.	Neuritis, recurring
1416	115	31.0	1.65		11.134	11.402	0.268	15.866			Periodontoclasia. Rarefying osteitis.	Proliferative arthritis.
1417	105	32.0			9.786	13.136	3.35	17.214			Periodontoclasia. Acute	Maxillary osteo-

FIGURE 131 CONTINUED (E)

1413	161 125	58 40	3.14 2.35		10.40 10.935	13.222 12.608	2.822 1.673	14.60 16.065			Locked apical.	Rheumatism. Nephritis.
797	119	49	2.86		9.640	11.802	2.162	3.582			Chronic periodontoclasia.	Lassitude.
335	87	32	2.34		8.721	10.067	1.346	6.879		32.53	Normal.	Nervous symptoms. Lassitude.
1414	100	29	2.17		9.600	9.960	0.360	4.067			Locked apical.	Heart. Lassitude.
1415	134	37.5	2.73								Periodontoclasia.	Normal.
1416	115	31.0	1.65		11.134	11.402	0.268	15.866		38.65	Locked and open apical.	Proliferative Arthritis.
1421	107	33.5	2.80		9.80	10.935	1.135	7.20		39.39	Periodontoclasia.	Lassitude.
1419	107	46.8			8.384	12.205	3.811	9.216		25.49	Locked apical.	Lassitude. Tension in head.
1425	147 115	27.0 30.6	2.08		8.87 9.152	9.44 10.678	0.57 1.516	8.73 9.848		26.32 27.16	Periodontoclasia.	Nervous tension. Albuminuria.
1424	127	22.6			8.285	9.585	1.300	16.715		37.84	Locked apical.	Nervousness. Acute digestive.
1423	154	28.5			10.315	12.727	2.412	10.685		35.56	Locked apical. Caries.	Goiter. Heart. Nervousness.
1311					11.670	13.22	1.550	7.76		29.75	Normal.	Deforming arthritis.
1324	102	23.0			8.428	10.672	2.244			20.36	Periodontoclasia.	Osteomalacia.
1381	76 95	29.0	2.29		10.600 8.790	12.360 10.263	1.760 1.473	16.400 7.210		23.00	Normal.	Rheumatism. Ulcers.
987	71	35.60	1.52		9.004	9.400	0.396	13.996		32.50	Normal.	Rheumatism. Heart. Eyes.
1417	127	33.7			9.045 9.84 10.935 10.142 10.314	10.270 11.171 12.340 11.564 11.278	1.235 1.336 1.405 1.422 0.964	15.995 6.429 12.340 8.058 9.686		34.7 30.15 34.68 30.16 30.50	Periodontoclasia. Acute apical abscess.	Maxillary osteomyelitis. Acidosis.
1424	125	29.1			9.173	10.986	1.813	17.827		29.90	Locked apical.	Acute digestive. Nervousness.

FIGURE 131 CONTINUED (F)

reading was not made after fasting as is required for a determination of hyperglycemia. When, however, such seemed indicated this was done.) non-protein nitrogen, uric acid, urea, acid-base balance, alkali reserve or a CO_2 combining power, also expressed as alkalinity index, ionic calcium, calcium pathologically combined, thrombin content, total calcium (including the ionic, pathologically combined, and the physiologically combined, such as calcium proteinates, etc.) It will be noted from reviewing this table that there is a very great variation in these different chemical constituents of the blood in the different individuals, and this very extensive study has involved the relating of these to the various pathological states, and particularly to the dental conditions and the changes in these and the physical symptoms or involvements, with the changes in the dental focal infection elements.

When, now, we relate the general clinical symptoms and physical conditions of these patients with these data, there are certain factors that we find quite universally associated. It will be noted, for example, that with few exceptions the high readings of blood sugar are found associated with high ionic calciums of the blood. While there are very few exceptions, this becomes an association which has a quite constant significance, as we will see. Another striking association is the practically universally high ionic calcium in cases of acute periodontoclasia. Similarly, certain types of susceptibility and involvement with rheumatism and neuritis, tend to be associated with a depressed ionic calcium of blood. We have, accordingly, divided these patients out into groups and studied them intensively in connection with these various factors, and have made a very large number of animal inoculations and subdermal tooth implantations, and checked these chemical changes of the blood against these established conditions. These will be reviewed in detail.

But these studies have tended to be quite indefinite with regard to the calcium, for some groups of individuals with approximately normal total calcium have included many cases with definite rheumatic group lesions, for while there was enough total calcium present it did not seem to be available for normal metabolic and catabolic processes. Another great difficulty has been the variation that has developed in the calcium determinations as made by different methods. It has been known for some time that calcium is present in the blood in two principal forms: ionic and combined, the latter including the various calcium proteinates. We have, accordingly, spent a great deal of effort to determine the amount of the ionic calcium as well as the total calcium and, where possible, the pathologically combined calcium for the various types of lesions. We have found that in a large percentage of cases of certain types of rheumatic group affections there is at the time of the active process a low ionic calcium; and, furthermore that as the ionic factor approaches normal, the symptoms disappear. In the coagulation of normal blood, calcium is a fundamental factor; but instead of ionic calcium's being taken up as might be anticipated in that process, it is, as a matter of fact, liberated, for the ionic calcium of the plasma of uncoagulated blood is lower than that of the serum of coagulated blood. (The fluid of the circulating blood is referred to as the plasma and the fluid which separates out from the coagulum of coagulated blood, as the serum.)

Normal blood should contain from 10 to 10.7 milligrams of calcium per 100 cubic centimeters. When the blood is in circulation, approximately four milligrams of the calcium are carried in combination with the thrombin, a little less than a milligram in the blood cells and about six milligrams as ionic calcium. In the clotting process the four milligrams in combination with the fibrinogen will be released in the process of the formation of fibrin and will appear as freshly ionic calcium in the serum. Accordingly, if, in any individual the total calcium be reduced four milligrams—namely, from ten milligrams to six milligrams—the four milligrams which are combined with the fibrinogen will not be available in the circulation as ionic calcium, and the total ionic will be reduced to two milligrams; in other words, in this case there is a reduction of two-thirds from normal, whereas the total calcium has only been reduced a little more than one-third.

From this it will be seen that determinations of the total calcium may be very misleading. No problem with which we have been engaged has compared in difficulty with this one of the making of dependable determinations of the quantity of calcium in different states in the blood. It will readily be seen that any incineration method can only give total quantities, since the ash can give no indication of chemical structure of destroyed compounds. Nor have we, as yet, dependable quantitative *chemical*[10] reactions that will differentiate with certainty the ionic calcium from the combined calcium though, no doubt, experimental methods will be improved very rapidly, to make this more easily possible. We have, however, *biological*[11] methods for making these determinations and we have, accordingly, depended on these.

Similarly, we have determined the amount of calcium pathologically combined in different stages of the treatment of a rheumatic group lesion. Figure 132 shows the progressive stages toward normal, of a case in which the pathologically combined is expressed. It will be noted from this chart that the ionic calcium began at 7.5, with a pathologically combined factor of 2.2. This patient was suffering from a recurring infective process for months after a mandibular extraction had been made under gas. No sequestra ever formed, and there was no direct evidence of an osteomyelitis. The condition came finally to involve the fascia and musculature of the neck and side of the face, with much enlargement of lymphatics, which ultimately required deep surgical drainage. Gauze packs were replaced daily for months, and the cellulitis tended to increase. The method of treatment will be discussed in detail in the chapters on the glands of internal secretion (Chapter No. 37) and methods for reinforcing a deficient defense (Chapter No. 42). The important thing in this connection is to note that with the progressive increase in his ionic calcium, whether as a cause or an effect, there was a marked improvement in his physical condition. From the 31st of August to the 13th of September (two weeks' time) there was an increase in

Important references. See bibliography for others.

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EFFECT OF TREATMENT ON IONIC CALCIUM OF BLOOD

Date	Hour A. M.	Treatment for Ionic Calcium	Ionic Normal Serum	Ionic Treated Serum	Comb. Pathological
8–31–22	9:00	Began	7.5	9.7	2.2
9– 6–22	10:00	Continued	7.9	9.9	1.9
9–13–22	11:00	Continued	8.1	9.5	1.4
9–26–22	11:00	Continued	8.2	9.4	1.2
1–24–23	11:00	Discontinued	10.6	11.0	0.3
2–16–23		Resumed	9.2	11.1	1.8
4–25–23		Continued	9.4	9.9	0.5

FIGURE 132.

the ionic calcium of the blood of 0.6 mg. per 100 cc., and a decrease in the pathologically combined of 0.8 mg. This patient had been in a process of decline for a couple of years and had been unable to carry on his work for many months, and with his age of fifty-seven and the seriousness of his disturbance, it seemed very probable that with his progressive and continuous decrease in defense with increase in the severity of his conditions, he was heading for a complete, and perhaps final break. With his low defense and the history of previous surgical procedures, which seemed to give only temporary benefit, hope for material assistance by that means was not indicated.

However, under treatment for the increase of his ionic calcium, his change was most rapid and remarkable. Not only did his state of impending doom give way to one of confidence and courage, but he gained in weight and physical endurance so rapidly that in a few weeks' time he was back to his office, carrying not only one man's work, but two or three, and notwithstanding his tremendous overload, went on gaining progressively as his ionic calcium increased; and in about four months it was up to normal, 10.6, and his pathologically combined had decreased to 0.3. His facial condition and neck involvement entirely disappeared spontaneously and never recurred. At this time the treatment was discontinued and in about three weeks' time his ionic calcium had decreased to 9.2 and his pathologically combined had increased to 1.8. The treatment was resumed and in nine weeks, notwithstanding an excessive overload and worry, his condition again improved, the ionic increasing to 9.4, and the pathologically combined (which is very important) decreased from 1.8 to 0.5.

It is a very common occurrence in connection with the study of these cases to find that accompanying the general physical depression there is a mental depression which I have termed "Mental Cloud", which varies in severity from a sense of impending doom to one of lack of courage. It is quite remarkable that this depressed mental state tends rapidly to disappear with the increase in ionic calcium toward normal. I have discussed this in further detail in the chapter on mental diseases.

Perhaps no phase of local and systemic involvement from dental infection is more frequently manifest than the disturbances of the circulation, both local and general, the most readily discerned of which, both by the patient and the operator, will be disturbances of coagulation; and it will be seen that these studies throw a flood of new light on secondary postoperative hemorrhages, bleeding gums, etc. This may either be a temporary expression or a quite general and extended one. It will also be possible for us to distinguish quite clearly between an hereditary hemophilia and a pathologically produced one. An extreme illustration of the latter will be seen in the following case.

Case No. 1084.—The patient was presented with a history of hemophilia so serious that he felt he was bleeding to death, and on several occasions his life had been despaired of. During the preceding two weeks he had had two transfusions to restore, if possible, the clotting ability of his blood. The hemorrhage was practically continuous from the gums, with occasional epistaxis. A tooth had been extracted three months previously and its socket was still bleeding. There was some hemorrhage from his gums practically every moment night and day. On a careful study of his case I observed that the hemorrhage was greatest around his non-vital teeth, none of which showed either extensive areas of absorption or were the least tender. (See Chapter 60) Inasmuch as I had several times had strains of organisms from dental sources that produced spontaneous hemorrhages in rabbits, I suspected that the teeth were providing some substance which was acting directly upon the blood, whatever other sources there might have been for his disturbance. He was barely able to walk; had to be assisted up all steps; was exceedingly weak and of ashen color. Notwithstanding the great danger attending an extraction, through the difficulty of controlling the hemorrhage, it seemed very desirable that his pulpless teeth be removed, both in order to relieve him from their injurious effect, if such existed, and to secure a culture for making a vaccine to reinforce his systemic defensive reactions. Great difficulty was experienced in controlling the hemorrhage following the extraction, a compress being required night and day for several days; and in spite of this, approximately 100 cubic centimeters of blood were lost in a few hours following the extraction. It is sufficient to state here that, with the use of a vaccine and the elimination of his dental infection his clotting time reduced progressively from eight and ten minutes at the time of the first extraction, to three and three and one-half minutes; and after the first extraction I had little trouble in controlling postoperative hemorrhage. In a week's time practically all spontaneous hemorrhage had ceased; and in four weeks' time he was carrying on his work approximately as normal.

But this is not the only important part of the history. Cultures grown from the interior of these teeth, and injected into a large number of rabbits, produced in many of them serious and early disturbances in the blood stream. Many had spontaneous hemorrhages and very marked change in the clotting time of the blood, even extending to ten minutes from a normal of from one-half minute to one minute and one-half. In the chapter on circulation disturbances there will be seen a series of cases, including this one, of spontaneous hemorrhages produced in rabbits when inoculated with the cultures from the teeth of patients suffering from hemophilia. One of the above rabbits inoculated with the culture from this case and shown in a later chapter referred to, died in twenty hours of spontaneous hemorrhage in the thigh and kidney, so profuse that although the effort was made promptly, we could not get enough blood from the heart and blood vessels to make a chemical analysis, a most unusual experience.

While the injurious effects of infections on the blood are by no means limited to the disturbance of the coagulation mechanism, this change is perhaps the most readily seen of any, and it is also very easily determined with instruments that are adapted for that purpose. It will be instructive, to note the progressive change in this patient. In the first three days after his first extraction, the clotting time decreased two minutes (from eight to six). He then had a slight reaction, and for three days it required seven minutes. In two weeks' time it had decreased two and one-half minutes to five and one-half minutes, and then decreased about a minute a week, reaching four minutes in about four weeks and three and one-half minutes in eight weeks. The spontaneous hemorrhages ceased the third day after the first extraction.

The chemical analysis of this patient's blood showed the CO_2 combining power to be 68, non-protein nitrogen 27, and blood sugar on one occasion 180, on another 158; the creatinin on one occasion 0.9, and another 1; blood urea on one occasion 8.4, on another 9.7; uric acid on one occasion 4.15, another 2.7; total calcium 8.16. At this time (April, 1921) we were not separating the calcium present in the blood in accordance with the amount present in ionic form, the amount pathologically combined and that physiologically combined, and total calcium. This figure would represent simply the total; and inasmuch as the total was reduced below the point of safety for the ionic alone, it is evident that this patient was in a state of very great calcium depression. Our later cases with our greatly improved method (though not as yet completely adequate and satisfactory) have thrown much additional light on these conditions.

A careful study of the data furnished in this case and several showing blood changes, which latter showed very marked improvement after the removal of infected teeth, led to the general conviction that the teeth in certain cases provided a substance which combined directly with the ionic calcium of the blood and removed it from availability, though remaining in the circulation. This is also very strikingly suggested by the very nature of both condensing and rarefying osteitis. In order to test this, we have made a series of studies of the effects of the extracted teeth on drawn blood of the patient from whom the tooth was extracted to determine its effect directly upon the available ionic calcium, and have found most important new data. Figure 133 shows a series of such teeth and the amount of depression of the ionic calcium

BLOOD CALCIUM CHANGES PRODUCED BY INFECTED TEETH

Case No.	Calcium			Tooth Placed in Serum			Decrease in Ionic		Total in Pathological Combination	
	Ionic	Ionic and combined	Pathologically combined	Ionic	Ionic and combined	Pathologically combined	Actual	%	Actual	%
1325	9.86	10.58	0.72	8.95	9.38	0.43	–0.91	–10	–1.63	15
817	9.89	10.13	0.24	8.66			–1.23	–13	1.47	15
1363	11.901	15.40	3.496	12.732	13.44	0.708	+0.828	+7	+2.66	17
1353	11.920	11.920		8.51	9.16		–3.41	–29	–3.41	28
1350	9.06	9.66	0.60	8.54	12.58	4.04	–0.52	– 6	–1.12	12
1404	11.802	13.334	1.532	7.258	11.802	4.544	–4.544	–38	–5.076	38
1267	8.10	9.53	1.43	6.05	8.13	2.08	–2.05	–25	–3.51	37
1315	5.25	7.50	2.25	1.25			–4.00	–76	–6.25	83

FIGURE 133.

produced in the blood of the patient from whom the tooth was extracted. It will be seen that some teeth produced practically no effect; most non-vital teeth of long standing, some effect; and some, very profound effect. For example in Case No. 1315, it will be seen that the ionic calcium of the blood was reduced from 5.25 mgs. per 100 cc. to 1.25. This patient was very ill, and the indications were very strong that her dental infections were seriously contributing to her illness. In this group we have several different types, and it is very significant that the teeth of the fourth, sixth, seventh, and eighth cases, which produced depressions in the ionic calcium of the blood of 25 per cent or more, the last 76 per cent, were taken from patients with a very marked evidence of physical injury, one expression of which was the symptoms of systemic involvements from dental infections. In only one case was there an increase in the ionic calcium (Case No. 1363), and in it the total ionic and pathologically combined was abnormally high, 15.4 mgs. per 100 cc., and it seems probable that the presence of the tooth in this patient's blood, carrying 3.49 mgs. of pathologically combined calcium, acted in some way on that element of the blood. In the last column we have added the original pathologically combined and the newly combined from the presence of the tooth, and it will be noted that in the last case of the original 7.5 mgs. of calcium, ionic and pathologically combined, in this patient's circulating blood after the patient's tooth was placed in the blood there was only 1.25 ionic available, or the total combined of this individual's blood after placing the tooth in it was 83 per cent. In the last column we have expressed in percentage that part of the calcium of the blood which should have been available but was in pathological combination: namely, the pathologically combined of the circulating blood plus the pathologically combined produced by placing the tooth in some of the freshly drawn circulating blood. It will be noted that these percentages run from 15 to 83, with four of the eight 28 per cent or over, with an average for the eight cases of 31 per cent.

It is, therefore, not surprising that if an infected tooth within one hour's time will seriously depress the ionic calcium, that the continued presence in the system of such a toxic substance must, of necessity, unless there be some powerful sterilizing agent, exert a very definite and serious influence on the blood. If, instead of a single tooth, the patient has several producing such a toxic substance and is not able to neutralize their products immediately about the tooth, grave systemic results should be expected to occur. It is, accordingly, just what should be expected, that so usually develops that when infected teeth are removed from the systems of patients suffering from depressed ionic calcium, that lesion automatically decreases or disappears. In another chapter on the glands of internal secretion I have discussed some phases of Nature's mechanism for neutralizing these poisons.

By studying the data in the next chart it is very readily seen that there is a constant relationship between the ionic calcium and metabolism, for continually with a decrease in ionic calcium there is a decrease in the weight. I have undertaken, therefore, to study this phase more exactly in order to determine, if possible, somewhat of the significance of the fact that patients suffering from dental infections tend so frequently to be underweight, and after the removal of these dental infections increase rapidly and materially. In the chapter on Marasmus and in the chapters of Part Two, I review cases with increases in weight ranging up to 50 per cent, with many of them increasing 10 to 25 per cent. This raises the question: To what extent is the depression of the weight below normal related to, or an expression of, the ionic calcium of the blood? To determine this and the associated factors we have made a series of implantations under carefully controlled conditions, where the weight has been checked carefully against the ionic calcium. A group of these is shown in Figure 134, entitled "Chemical Changes in the Blood, Produced by Implanting Infected Teeth Subdermally, and the Relation of the Changes of Ionic Calcium and Body Weight." In this chart we show six rabbits. In the first there was a decrease in the ionic calcium of 50 per cent, produced by the placing of the patient's tooth beneath the skin of the rabbit, and all this occurred in four days' time. There was, accordingly, not an opportunity for great wastage of the animal's body, death ensuing before the depletion of the tissues. The total loss in weight in this case was 17 per cent. In the second case the decrease in ionic calcium was 1.18 grams or 12 per cent. But this extended over a period of sixteen days, which gave greater opportunity for depletion of the body tissues, the actual loss of weight being four hundred seventy-one grams, or 34 per cent. In the third rabbit the period taken for the tooth to kill the rabbit was shorter—namely, three days—the ionic calcium loss being three

CHEMICAL CHANGES IN THE BLOOD, PRODUCED BY IMPLANTING INFECTED TEETH SUBDERMALLY, AND THE RELATION OF THE CHANGES OF IONIC CALCIUM AND BODY WEIGHT

Rabbit No.	Date	Weight	Weight Loss		Calcium plus Thrombin	Calcium Ionic	Calcium Ionic plus Combined	Calcium in Combination	Calcium Ionic Loss	
			Actual	%					Actual	%
1106	A. 2-16-23	1141			14.78	10.88	11.78	0.90		
1106	B. 2-20-23				11.27	7.00	7.00	0.0		
1106	C. 2-20-23	942	**199**	**17**	9.80	5.41	6.09	0.68	**5.47**	**50**
1145	A. 3-27-23	1381			14.50	10.13	10.13	0.00		
1145	B. 3-28-23				13.88	8.89	11.67	1.77		
1145	B. 3-30-23				16.80	8.95	11.23	2.28		
1145	C. 4-13-23	910	**471**	**34**					**1.18**	**12**
1099	A. 2-13-23	1822			14.80	11.00				
1099	B. 2-14-23	1483			13.2	9.92	10.36	0.44		
1099	B. 2-14-23	1385	**437**	**24**	18.5	11.22	10.82	0.40		
1099	B. 2-16-23				10.19	7.91	9.00	1.99	**3.09**	**28**
1108	A. 2-20-23	1265			17.00	10.59	12.61	2.02		
1108	B. 2-22-23	1185	**80**	**6**	18.40	8.84	13.00	4.16	**1.75**	**17**
1109	A. 2-20-23	1375			17.20	9.88	10.37	0.49		
1109	B. 2-22-23	1256	**119**	**9**	17.80	7.82	9.80	1.98	**2.06**	**21**
1080	A. 1-27-23	1478			16.50	8.90	8.90	0.00		
1080	B. 1-29-23	1360			10.17	7.12	7.12	0.00		
1080	B. 1-31-23	1321			7.74	7.25	8.69	1.44		
1080	B. 2- 1-23				11.80	7.99	8.56	0.57	**0.91**	**10**
1080	B. 2- 3-23	1210	**268**	**19**	19.00		12.74			

FIGURE 134.

A—Readings before tooth implantations.
B—Readings after tooth implantations and before death.
C—Readings after death.

grams, and the total loss in body weight four hundred thirty-seven grams, or 24 per cent. Similarly, the other three rabbits shown in this chart, reveal calcium losses of 17, 21, and 10 per cent respectively, with body weight losses of 6, 9, and 19 per cent in two days each for the first two and six days for the last. This shows clearly that there is a time factor involved, and seems to emphasize the profound effect on metabolism, in general, of introducing into the animal's body a toxic substance which directly disturbs the ionic calcium. The data available do not justify the conclusion, however, that no other important factors are directly involved, nor that the calcium decrease is the chief or only factor interrupting the metabolic process.

Studies were then made to determine the nature of this calcium compound. If it were an insoluble salt it could be removed by filtering or centrifugation or settling. It was found, however, not to be removed by an ordinary Berkefeld filter or by centrifugation. The chemical bond was evidently a very loose one, (though enough to take the ionic calcium out of service) since it could be again separated with sodium hydrate and the ionic factor of the blood serum restored approximately to normal.

In order further to study this factor, we have injected normal rabbits, to determine the effect of various cultures in reducing the ionic calcium. These are shown in Figure 135.

COMPARISON OF CHANGES IN IONIC CALCIUM AND BLOOD MORPHOLOGY, DUE TO CULTURE INOCULATIONS

Date 1923	Hemoglobin	Erythrocytes	Leucocytes	Polymorphonuclears	Lymphocytes		Basophiles	Arneth Index	Ca and Thrombin	Calcium Ionic	Ca Ionic and Combined	Calcium in Combination
					Large	Small						
6-1*	85	6,900,000	15,000	**57**	7	**34**	2	83	15.20	**11.53**	13.00	1.47
6-2	85	6,150,000	27,700	**70.1**	14.4	**15.4**		48	17.20	**11.80**	13.22	1.42
6-4	80	5,750,000	19,800	**35.5**	8.8	**53.3**	2.4		15.00	**9.45**	13.66	4.21
6-5	80	5,800,000	16,600	**64.7**	16.8	**17.9**			17.00	**8.46**	8.71	0.25
6-6	85	5,100,000	14,800	**31.2**	6.4	**62.4**			17.40	**8.05**	9.80	1.75

FIGURE 135.

*Before inoculation. (Case No. 1406. Rabbit No. 1221.)

Another research was established to determine further the effect of infected human teeth in reducing the normal ionic calcium of the blood stream, by placing the patient's extracted tooth beneath the skin of a rabbit. This has disclosed a very remarkable result, as shown in the table in Figure 136.

This chapter is supposed to deal with chemical changes of the blood in relation to dental infections. There are so many elements and compounds in the blood that this subject could be

DEPRESSION OF IONIC CALCIUM BY IMPLANTING INFECTED TEETH

Case No.	Rabbit No.	Date	Weight	Weight Loss		Ionic Calcium			Pathologically Combined	
				Actual	%		Actual Loss	% Loss		Increase
404	1118	3- 5-23 3- 7-23	1153 1140	13	1	**11.06** **9.84**	1.22	11	0.00 1.16	1.16
1353	1107	2-20-23 2-23-23 2-26-23	1069 1020 846	223	21	**10.76** **11.74** **9.52**	1.24	11	2.11 0.48 3.92	1.81
1371	1145	3-27-23 3-28-23 3-30-23	1381			**10.13** **8.89** **8.95**	1.18	12	0.00 1.77 2.28	2.28
1317	1099	2 -13-23 2-14-23 2-14-23 2-16-23	1822 1483 1385	437	24	**11.00** **9.92** **11.22** **7.91**	3.09	28	0.44 0.40 1.99	1.55
1317	1108	2-20 -23 2-22-23	1265 1185	80	6	**10.59** **8.84**	1.75	17	2.02 4.16	2.14
1317	1109	2 -20-23 2-22-23	1375 1256	119	8	**9.88** **7.82**	2.06	21	0.49 1.98	1.49
1317	1074	1-17 -23	1925 1552	373	20	**12.37** **6.83**	5.54	45	0.64 0.6	

FIGURE 136.

extended to cover an entire volume. Referring again to Figure 131 of this chapter, we find that just as calcium has been a very variable factor, similarly so have several other substances. It is particularly important in the study of these to note their relation to each other; and, accordingly, you will note the incidence of a hyperglycemia to the calcium factors, total and ionic. It is not an accident, in referring back to the composite table, that where calcium reads very high the sugar of the blood is very high. We have, accordingly, studied the effect of dental infections and the relation of the types of dental infection to the different types of diabetes. A very important new light has been thrown on the whole problem of carbohydrate metabolism and sugar retention in the blood by Banting, Best, Collip, Hepburn, and Macleod, working at the University of Toronto, to whose work there are many references in the current literature.

It is not necessary to review here that, glycosuria, or the presence of sugar in the urine, is not of itself an evidence of hyperglycemia. Formerly, distinction was made between a true and false diabetes, the latter being cases in which there was the presence of sugar in the urine without serious harm to the patient. It is now recognized, particularly due to the work of Hamburger, that an increase in ionic calcium in the blood makes it possible for the kidney cells to let through a quantity of sugar where little or no sugar would pass with the slightly lower ionic calcium.

While the pathology and etiology of diabetes are not completely established, it has been interesting to note that in many cases the quantity of sugar in the blood has decreased following the extraction of infected teeth, and this disregarding in large part the variations and uncertainty of the significance of decrease of the sugar in the urine, which is a very common sequence to extractions. Such a case is shown as follows:

The culture grown from the tooth of Case No. 1195, when inoculated into rabbits, raised the blood sugar in nineteen days from 97 to 149, which, seven days later, had subsided to 121, and in twenty-six days still later to 92, five below the resting normal of this rabbit before inoculation. The rabbit was given another inoculation of this same culture, which, however, had been retained in the artificial medium, and on this occasion the same dosage increased the blood sugar to 105. This patient's resting blood sugar was 130 mgs. per 100 cc. and the urine sugar 430, or 4.3 per cent. This patient from whom the tooth was extracted and whose urine sugar was 430 before the extraction of the tooth, had the same reduced so that on two subsequent determinations, (the first one in eleven days,) no sugar was found in the urine, and in two years' time, the reports that she has brought to me have been that her physician has made frequent determinations and has not found sugar.

One of these patients' blood sugar reduced from 285 to 235 in twenty-four hours (probably a temporary change) after the removal of dental infections. He had no suspicion that he had diabetes. When advised to change his mode of living, and particularly to put himself under a strict program prescribed by a good internist, he advised that his business affairs would not allow of any change in his program for some months. This patient's urine sugar was 542 mgs., or 5.4 per cent. That this disturbance was progressive and very serious was evidenced by the fact that twenty days later it was 1100, and at this time we again urged that he put himself in the care of a skilled internist. It is important and pathetic to note that he was buried before that time. The importance lies in the fact that people can be in so serious condition and not have any knowledge or suspicion of it, and again may take the matter with so little concern, depending entirely upon their feelings which may be so misleading.

However, some individuals are capable of carrying a surprisingly large excess of sugar in the blood for considerable length of time. For example, Case No. 1268 has had blood sugar ranging from 295 to 410 mgs. per 100 cc., and a urine sugar ranging from 306 mgs., or 3 per cent, to 446 mgs., or 4½ per cent, for over a year, and while it has materially improved since the removal of a number of infected teeth, the glycosuria and polyuria persist. He feels so much better that he refuses my urgent recommendation that he be placed in the hands of a first class internist for direction of his diet. Fortunately, many of these individuals are continuing into a period when there is more hope for their assistance through the use of insulin and other pancreatic preparations.

Accepting the threshold of probable danger for the human as 120 mgs. of sugar, after fasting, per 100 cc. of blood, it is quite striking to find some sugars in our list going to 400, and, yet, the patients were not aware that they had diabetes. These are discussed from the clinical standpoint in Chapter 63. We will also discuss in Chapter 53 (on theoretical discussion) the significance of the type of gingival pathology which accompanies diabetes.

There is a phase of the role of ionic calcium which must be stressed. While the evidence available strongly suggests that certain rheumatic susceptibilities and conditions tend to develop in the presence of a low ionic calcium of the blood, it is equally evident that certain types of rheumatism develop in the presence of a high ionic calcium. While these seem to be associated with a different type of rheumatic symptoms and bone changes, the data available do not yet justify an attempt at classification that will be expected to be final, though it may be very suggestive. I speak of this at this point to forestall hasty conclusions and unwarranted deductions. In general, we may associate divergences from normal in ionic calcium of the blood with general types of lesions somewhat as follows:

Normals tend to have a mean of approximately 10 to 11. Condensing osteitis and lowered defense to rheumatic group infections seem generally to be associated with a lowered ionic calcium (6.9). A good defense shows a high normal ionic calcium. Active periodontoclasias and pyorrhea show an abnormally high ionic calcium (10.7-12.5). Individuals with a low ionic calcium do not have, while in that state, a tendency to extensive alveolar absorption. Patients with large apical areas of absorption have a high or normal ionic calcium; patients with relatively small apical areas, a low ionic calcium. Individuals whose teeth are sore, or have fistulae with recurring inflammatory processes, have normal or high calcium; those with low calcium have little or no local reaction and evidence, as pain about teeth which are infected. There are certain associations too: Patients with glycosuria and hyperglycemia, or the latter without the sugar appearing in the urine, or even those with sugar appearing in the urine without its being above the threshold which would term it "True Diabetes" tend to have a calcium higher than normal. I have discussed these various associations of calcium with the various pathological states in succeeding chapters.

URIC ACID.

A study of Figure 131 shows a variation in the quantity of uric acid present in the blood of the various patients there recorded, ranging from 1 to 7 plus mgs. per 100 cc. Various textbooks give us a normal of 1 to 3. A study of cases before and after removal of dental infections has shown a reduction of uric acid following the removal of dental infections. For years an important theory as to the etiology of rheumatism has been the increased uric acid of the blood. It is, however, now claimed by eminent authorities that, while certain of the rheumatoid group of symptoms—namely, gout,—have definite etiological relation to uric acid content of the blood, the other types do not have this direct relationship and the uric acid factor may vary through considerable range either coincidentally or independently.

ACID-BASE RELATIONSHIPS IN THE BLOOD.

It has been known for some years that while the hydrogen ion concentration of the blood varies but slightly from normal, this fact is only possible because of the very efficient buffer system contained in the blood, which has made possible quite wide variations in acid and alkali production without considerably disturbing the actual hydrogen ion concentration. It has similarly been known that the CO_2 tension in the alveoli of the lung automatically controls the rate of respiration, a practical illustration of which has been the necessity for a certain amount of re-breathing with nitrous oxygen and oxygen in order that the presence of the CO_2 may normally control respiration. In the system carbohydrates are oxidized at a rate which is determined largely by this acid base (or alkali reserve) relationship, which rate is directly influenced by hyperfunction of the thyroid. This condition of unbalance constitutes an acidosis. This has been determined or measured quantitatively by determining the amount of oxygen consumed, and of carbon dioxide given off in respiration during periods of rest and of fasting for from six to twelve hours. We have made a number of determinations on rabbits to ascertain if dental infections seriously disturb this basal metabolic rate, the animals being placed within the chamber connected with the metabolism machine. We have developed important data by this method but have found it a very laborious and tedious one. Several factors enter into this determination which cannot be controlled in rabbits as they can in the human. If the particular animal under study has been used to being handled and watched, the problem of excitability and fear will be reduced to a minimum, whereas in other animals, either because of lack of handling or a normal instinct of alarm and fear, these elements will completely change its rate of breathing and therefore its metabolic rate. That this is true is evidenced by the considerable variation in the readings that may be gotten with a given rabbit under different conditions of excitement. Another method—namely, that of directly reading the Ph with a potentiometer—is also very tedious because of the involved difficulties in maintaining the same CO_2 tension as obtained in the drawn blood, which cannot be allowed to come in contact with air, or be breathed upon by the operator.

The discussion of the acid-base balance and alkali reserve will be found in Chapter 44, Calcium and Acid-Alkali Balance.

SUMMARY AND CONCLUSIONS.

From these data it is apparent that very important chemical changes are produced in the blood from dental infections, and such as are far-reaching in the processes of metabolism and function. One of the very conspicuous changes is the disturbance of ionic calcium and the presence in the blood of a pathologically combined calcium. Since cell activity, both metabolic and catabolic, is dependent largely upon a normal ionic calcium in the fluids at the cell boundaries, very minute changes may produce very important physical disturbances, as, for example, the kidneys' permitting sugar to pass through when the ionic calcium gets above the normal limits. We would summarize some of the important chemical changes briefly as follows:

(1) Dental focal infections tend in many instances to lower the ionic calcium of the blood. (The fact and significance of a high ionic calcium in periodontoclasia are discussed in Chapters 45 to 56.)

(2) The placing of certain infected teeth in the blood serum of patients suffering from certain rheumatic group disturbances tends markedly to lower the ionic calcium of that serum.

(3) There is frequently found in the blood of individuals suffering from rheumatic group lesions, a reduced ionic calcium state and also a measurable pathologically combined calcium, which progressively disappears after a patient returns to normal.

(4) The placing of a patient's infected tooth beneath the skin of a rabbit tends similarly to reduce the ionic calcium of its blood. (The relation of these to the endocrine system is discussed in that chapter, No. 37.)

(5) Injection into the circulation of animals of the organisms grown from the teeth which produce these changes in the blood, tends also to reduce the ionic calcium of the animal's blood.

(6) The presence of dental infections tends in many instances to change the alkali reserve of the blood of patients; and when these teeth are placed under the skins of rabbits, they tend also to change their alkali reserve.

(7) Dental infections in some instances change the blood sugar content of the patient, as evidenced by the return to normal after the removal of dental infections, and the increase in blood sugar in animals, by injecting them with the culture from such teeth.

(8) The uric acid content of the blood varies considerably with the presence or absence of dental infections, particularly in cases of gout. It may, however, be very slightly changed in many cases of definite rheumatic group lesions, and its variation in the blood is very closely paralleled by its presence in the saliva.

Dental focal infections tend to produce, in many instances, one or several chemical changes in the blood, which changes tend also to be produced in animals when an infected tooth is placed beneath its skin; and, similarly, with certain methods of inoculation with the culture grown from these teeth. Some of the changes most frequently found involve:

(a) **The ionic calcium of the blood.**

(b) **The presence of a pathologically combined quantity of calcium in the blood.**

(c) **A reduction of the alkali reserve of the blood.**

(d) **The development of acidosis.**

(e) **An increase in the blood sugar.**

(f) **An increase in the uric acid.**

(g) **The development of nitrogen retention.**

(h) **The development of products of imperfect oxidation.**

CHAPTER XXI.

CONTRIBUTING OVERLOADS WHICH MODIFY DEFENSIVE FACTORS.

PROBLEM:—What are the contributing factors causing a break in resistance?

EXPERIMENTAL AND DISCUSSION.

We have looked upon dental infections as being sufficient or insufficient to produce the disturbances under consideration. This series of studies has been made to ascertain what, if any, are the factors which may be associated with dental infections and produce, or aid in producing, the break in resistance which expresses itself in systemic, as well as local disturbance. In a previous chapter, No. 4, we studied the basis on which human beings are comparable and found that, in the main, they may be divided into three groups with regard to their susceptibility to rheumatic group infections: namely, absent susceptibility, acquired susceptibility, and inherited susceptibility. In this chapter we desire to study the contributing factors to susceptibility by modifying the defense of the individual. These, we find, naturally divide themselves into two groups: namely, those which tend to make people with a normally high defense become susceptible in some tissue; in other words, changing a person from an absent susceptibility to an acquired susceptibility classification; and second, the forces which control in a case of inherited susceptibility and tend to make some particular tissue susceptible in that family.

An analysis of our collected data reveals that a very large number of individuals develop their rheumatic group lesions either as a complication with influenza or quite early following it. This will include not only rheumatic group lesions, more strictly speaking, but also bacterial invasions of other types such as tuberculosis and pneumonia. This latter, however, probably should, under these circumstances, often be considered as a rheumatic group lesion since it is often a systemic expression of streptococcal involvement already focal in the body. To determine this more exactly, I made a very careful study of influenza patients in five hospitals, three in this city and two in Columbus, in the epidemic of 1918. This was an exceedingly difficult study to make for several reasons: First, the patients involved were frequently too ill to be questioned with sufficient care to bring out all the data; and second, it was not possible to make roentgenographic studies, and many cases of dental infections were undoubtedly overlooked since only those were included, which were sufficiently gross to be determined definitely by oral examination, palpation, etc. A study of two hundred sixty influenza patients in five different hospitals, Figure 137, disclosed that when the patients were divided into two groups—those with, and those without clearly demonstrable dental infections—the percentage of individuals developing serious complications (in which we included pneumonia, empyema, carditis, severe neuritis and severe rheumatism) was found to be in the group without dental infections 32 per cent, and in the group with serious dental infections 72 per cent. Several factors should be carefully noted: In the pneumonias, the tendency to strangulation following coughing spasms, as a result of the bronchial exudate, produced violent inspirations which draw into the lung, fluids and infections from the mouth. This makes gingival infections a very marked contributing factor to the development of pneumonia. In general, however, the so-called locked infections (by which we mean those at root apices without opportunity for drainage into the oral cavity, which therefore must drain into the system, into the lymphatic and hematogenous circulations) are more to be feared since the system must of necessity become invaded from this source, with a breaking down of the local defense which has tended to wall off and defend the patients in times of their normal defense.

In our studies of this series we have found that, in the patients who have kept their mouths in good condition, free from gingival and apical sources of infection, both the incident of influenza itself, and complications with the influenza, are much lower than in the patients with extensive dental infection. This fact has also been reported to me by other dentists.

These general observations, together with the observations made in private practice, seem to demonstrate that the individuals, who carry focal dental infections with apparent safety during the period of their normal health, immediately are endangered, and very seriously so, when they are attacked with influenza

ORAL INFECTIONS AND INFLUENZA COMPLICATIONS

Hospital	Date	No. of Flu Cases Studied	Flu Only	Flu with Various Complications	Flu with Pneumonia	With Oral Infection			Without Oral Infection		
						Total	Flu Only	Flu with Complications	Total	Flu Only	Flu with Complications
1 Lakeside, Cleveland Men's Ward	Nov. 30	20	13–65%	7–35%	7–35%	8–40%	2–25%	6–75%	12–60%	10–83%	2–17%
2 Lakeside, Cleveland Women's Ward	Dec. 1	6	1–17%	5–83%	5–83%	5–83%	1–20%	4–80%	1–17%	0	1–17%
3 St. Francis Columbus	Dec. 4-5	23	5–21%	18–78%	9–48%	18–22%	3–17%	15–83%	5–78%	2–40%	3–60%
4 Grant, Columbus Nurses	Dec. 5	50	41–82%	9–18%	2–4%	0	Held certificates from dentists		50–100%	41–82%	9–18%
5 Grant, Columbus Private Patients	Dec. 5	51	38–74%	13–26%	8–16%	0	None known		51–100%	38–74%	13–26%
6 City Hospital Cleveland	Dec. 7	26	8–31%	18–69%	15–51%	23–88%	7–30%	16–70%	3–12%	1–33%	2–67%
7 Mt. Sinai Cleveland	Dec. 19	31	14–45%	17–54%	10–32%	21–68%	8–38%	13–62%	10–32%	6–60%	4–40%
8 Mt. Sinai Cleveland Nurses	Dec. 16	53	38–72%	15–28%	13–24%	0	Clean mouths		53–100%	38–72%	15–28%
Eight Sources		260	158–61%	102–39%	69–26%	75–29%	21–28%	54–**72**%	185–71%	136–68%	49–**32**%
Private Practice Patients		37	14–38%	23–62%	14–23%	37–100%	14–38%	23–62%	0		

FIGURE 137.

infection. In order further to test this problem, I have in the succeeding epidemics made inoculations into the tracheae of rabbits of the washings of the nasopharynges of the Flu patients, and have made comparative tests to determine whether or not these rabbits were more susceptible to focal infection. Figure 138, lower view, shows a reproduction in natural color of the lungs of a rabbit dying from pneumonia, as illustrating this condition. A rabbit was inoculated intratracheally with the washings from the nasopharynx of a Flu patient during the first twelve hours after the attack. This rabbit showed a depression in its mononuclear blood cells, typical of the influenza involvement, and was less active following the injection, with loss of appetite. (Rabbits so inoculated recover in a few days.) It was killed, and its lungs removed and macerated in normal salt solution, which washing was injected intratracheally into other rabbits. These developed the same general symptoms. The lungs of this rabbit are shown in Figure 138, upper view. Of the two injected intravenously with small quantities, ½ cc. of a 24-hour culture from dental infection, this one died of pneumonia (Figure 138, lower view). This experiment was made in the epidemic of February, 1923. A similar observation was made in the epidemic of 1922. A rabbit was injected intratracheally with the washings from the nasopharynx of a patient suffering from influenza, followed by the intravenous injection of a dental culture. This rabbit developed typical streptococcal pneumonia. A section of the lung is shown in Figure 139. Similarly, we have found that, when infected teeth are planted beneath the skins of the rabbits, they sometimes develop acute and terminal pneumonia. (See Chapter 61.)

PREGNANCY.

An analysis of the sex in Figures 42 and 47 in Chapter 4, reveals that the increase in the prevalence and severity of rheumatic group lesions shows a continued increase toward the female sex. A further analysis of these data reveals that in a great many instances, the acute attack of rheumatism dates directly to the time of pregnancy and lactation. The usual age of first rheumatic group involvement is between twenty and thirty-five in females.

Since so many young mothers, or expectant mothers, have developed acute rheumatism, heart, or other rheumatic group lesions, during the period of gestation or lactation, we have come to recognize this as one of the most important overloads which

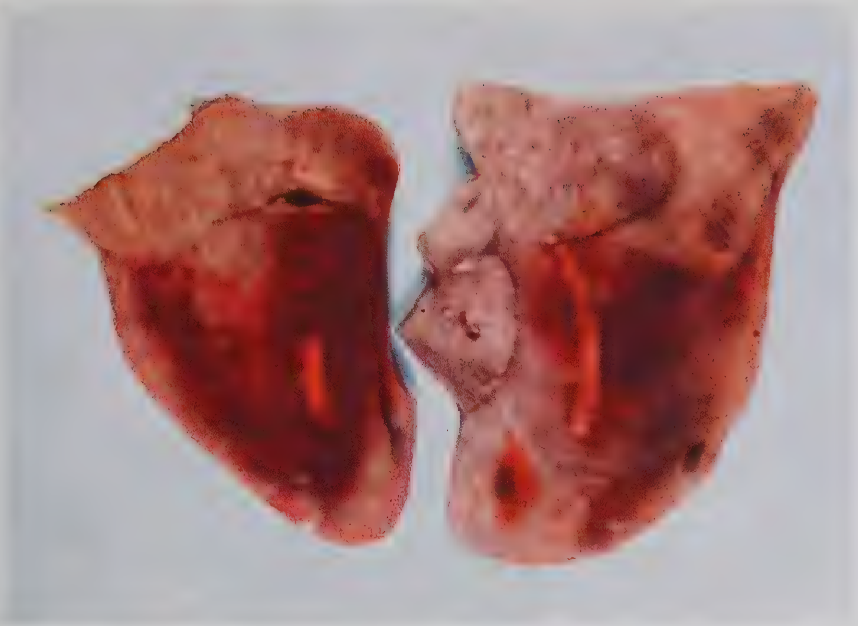

Figure 138-A. Influenza Lung of a Rabbit inoculated intratracheally with nasal washing from a flu patient. This is not fatal to rabbits.

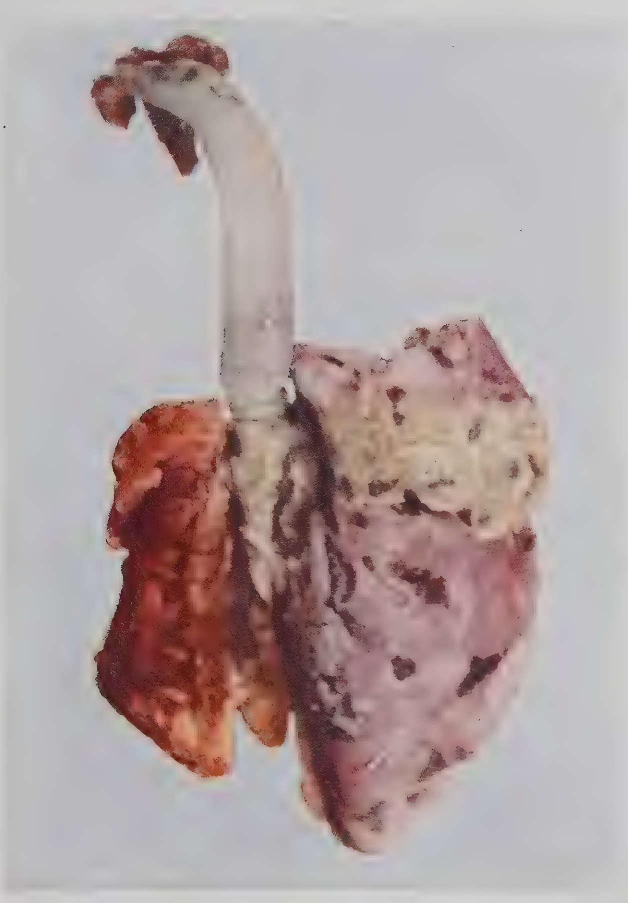

Figure 138-B. Fatal Streptococcal Pneumonia from injecting dental culture intravenously into rabbit with influenza.

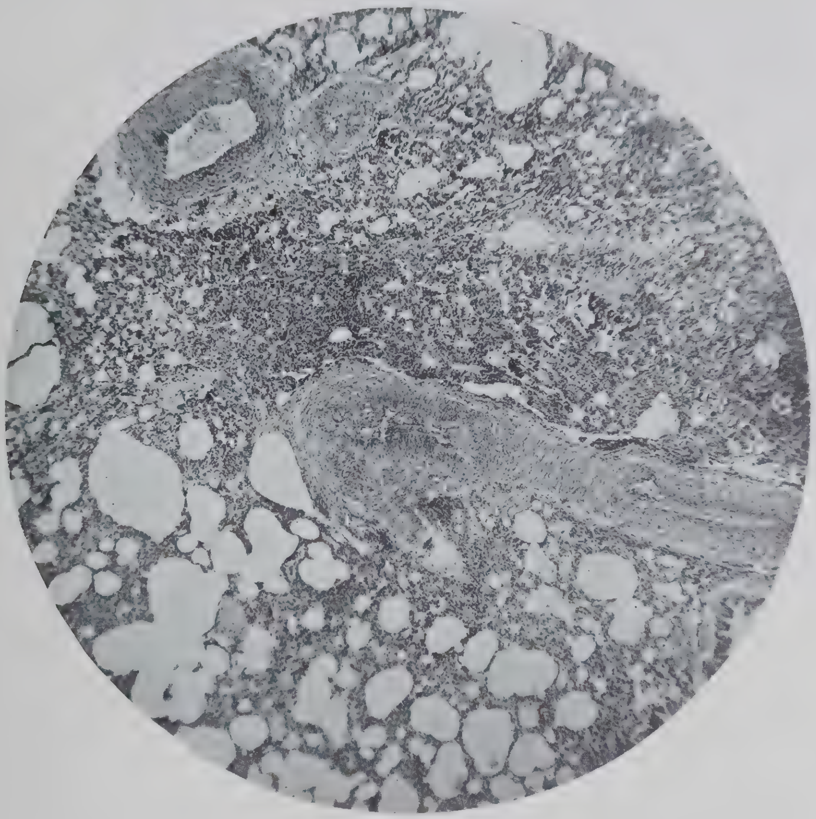

FIGURE 139. SHOWS A SECTION OF THE LUNG OF A RABBIT WHICH DIED OF STREPTOCOCCAL PNEUMONIA FROM A DENTAL CULTURE. THE BRONCHIOLES ARE OBSTRUCTED BY THE THICKENING OF THEIR LINING MEMBRANES AND BY THE EMPHYSEMA.

we have to consider. To illustrate:

A young married woman of twenty-two years undertook the responsibilities of motherhood with a physique and physical reserve which would be expected to be well above the average. In childhood she had had a mild endocarditis which left a mitral leakage. She also suffered from acute rheumatism, having had two quite acute attacks. After the birth of her babe, which was unusually robust, and during the early period of lactation, she developed such severe rheumatism that she could not wait on herself or the baby. A couple of infected teeth were removed and she immediately improved, though her relief was not complete. She ceased nursing her child in about six months, and immediately her remaining rheumatism disappeared. During the time of lactation she had been drinking large quantities of good milk.

We have seen this clinical picture over and over, and decided to make a test on rabbits. Accordingly, the following experiment was made. A rabbit referred to in Chapter No. 66, which had developed a complete paralysis posterior to the first lumbar vertebra, with loss of continence of urine and fæces, and complete loss of all sensory and motor control of the posterior region, and which had recovered so completely as to be apparently normal, except for a slight atrophy of a few groups of muscles, which caused a rotation of one hind leg, as shown in illustration, and which had gained in weight from 1025 grams to 1600 grams, was tested for the effect of maternity on its resistance to the residual infection. The roentgenograms showed both the location of the lesion and its structural change. The rabbit itself is shown in Figure 140, the roentgenogram of the spine in Figure 141, and a section of the repaired lesion about nine months after the original inoculation and the first development of the lesion of the spine. At the beginning of gestation, this rabbit was apparently in exceedingly good physical condition. It was fat, its coat sleek, and in every way seemed normal. It went through term with apparently no untoward symptoms. Five young were born, which seemed, at birth, to be developed normally. They all died in from a few hours to one and one-half days. She did not have the continued overload, therefore, of lactation. Prior to their birth and following, she was observed to be very nervous, easily frightened, and excitable. Her nervousness increased in severity and she began losing in weight, finally developing a very marked disturbance of the central nervous system, with choreic motions, rotation of the head with the least excitement, and she became so nervous that if the hands were clapped very hard near her, she would fall over on her side. She died in about five weeks' time with a terminal pneumonia which, on culturing, showed a streptococcus and diplococcus similar to that found in the lesions and similar to the organism injected, and originally secured from a tooth. Under another chapter, we will speak of pregnancy complications. It is my opinion that the lesion in the spine, though healed, retained the same type of infection which had originally been injected into the rabbit and which produced the spine lesion; that, at the time of lowered resistance, this organism about which Nature had been able to build a barrier, became rampant, again affecting first the overloaded nervous system, and later became focal as pneumonia.

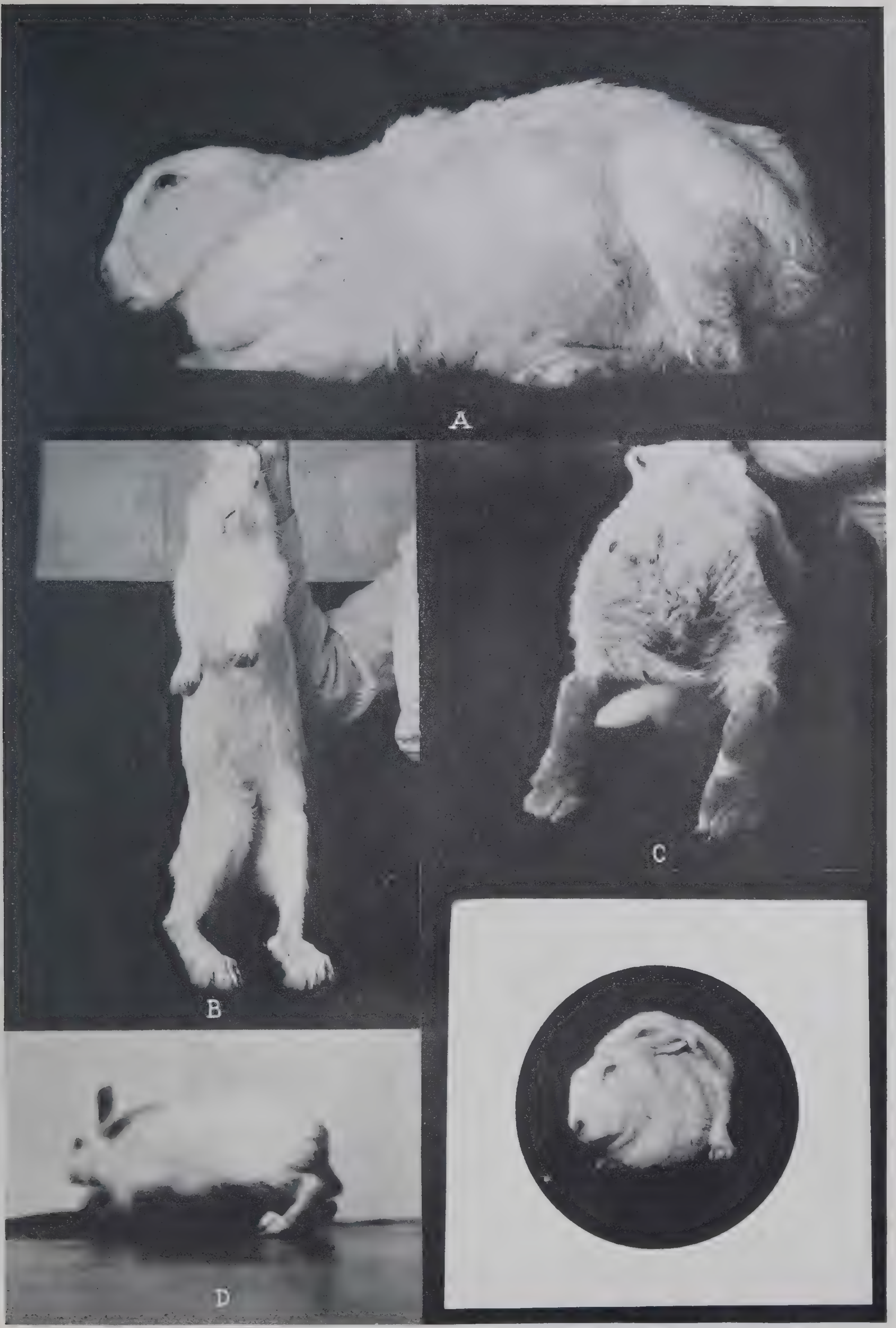

FIGURE 140. A RABBIT IN WHICH COMPLETE PARALYSIS WAS PRODUCED FROM THE CENTER OF THE SPINE BACKWARD, BY DENTAL CULTURE INFECTION. IT APPARENTLY RECOVERED ALMOST COMPLETELY EXCEPT FOR ATROPHY OF A FEW MUSCLES WHICH PRODUCED A TWISTED LEG.

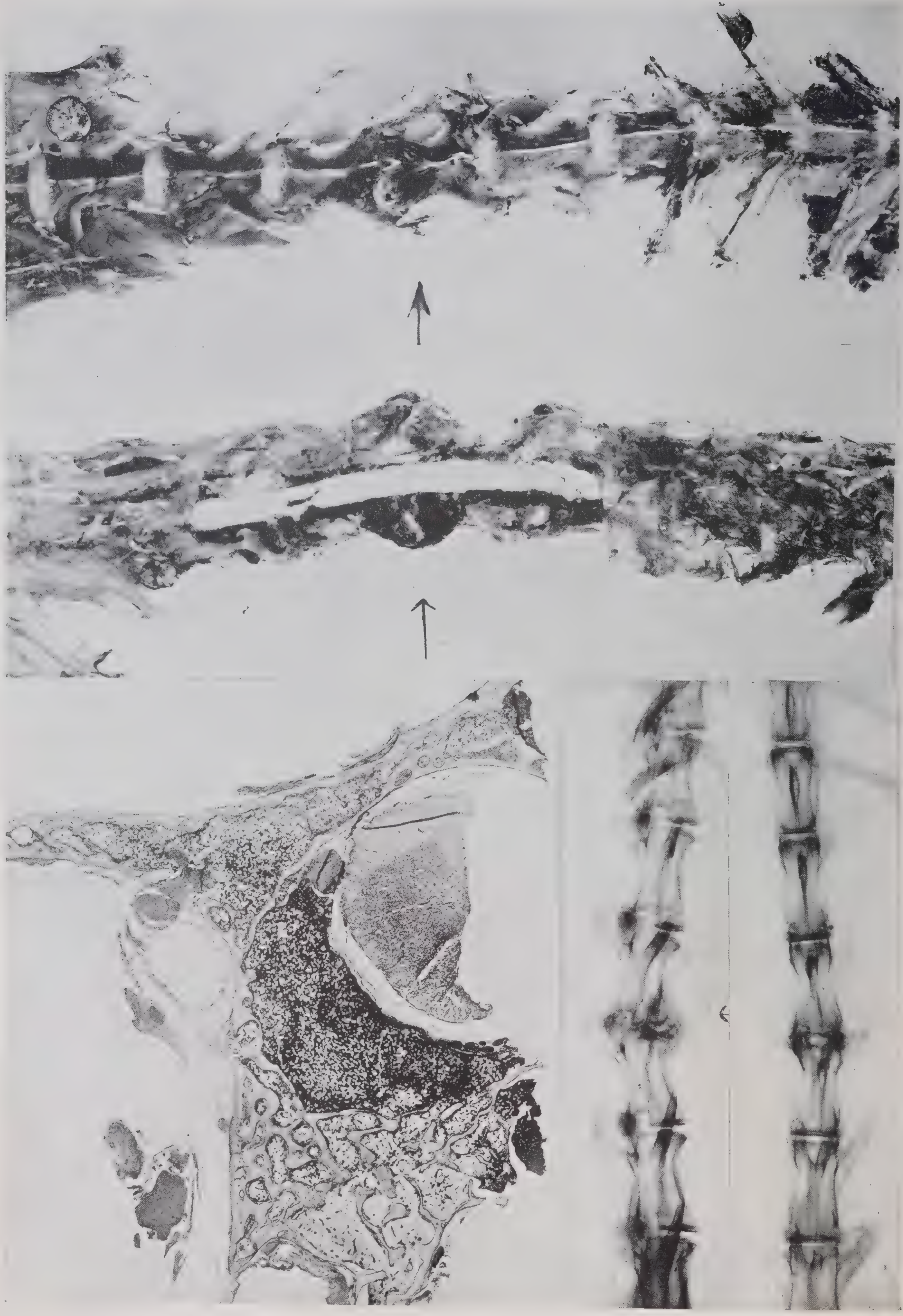

Figure 141. Views and sections of the spine of rabbit shown in Figure 140. Note destruction of intra-vertebral cartilage in A and B; destruction of body of vertebra in C; and mild condensing osteitis in D and E.

TRAUMA.

Acute irritations producing an active inflammatory process would seem to increase, or at least not reduce, the local defense of most tissues; whereas, a continued irritation tends to reduce the resistance of the tissue involved and make it more susceptible to infective invasion. To illustrate:

A man who had been on shipboard in passage from the Philippines to this country, following which he was on the train from San Francisco to Cleveland, all of the time without much exercise, secured a position as floor walker or night watchman in a manufacturing plant, having acres of cement floors, requiring several miles of walking for his beat to ring in the record of his rounds. He wore shoes without rubber heels. The irritation to the synovial membranes at first gave him a sense of discomfort, which was relieved by resting. After continuing the irritation for a few weeks, he was afflicted with acute rheumatism in the joints receiving the thrust. During all of this time he had had chronic dental infections. The removal of the dental infections, together with the use of rubber heels, relieved the synovitis and he was able to continue in the same occupation.

Similarly, eye strain makes the eyes much more susceptible to irritation from dental infection. Figure 6, Chapter 1, illustrates the dental condition of a patient who had such a disturbance. He had suffered for several years from the difficulty of not being able to read for long periods, a condition which was helped by periods of rest but not entirely relieved. It was also helped, but not relieved, by glasses. The removal of his dental infections made it possible for him to discard his glasses which he had worn for fifteen years, and made it possible for him to read without limit and without discomfort. We have had many cases where the patients have reported to us, after the removal of their dental infections, that they did not longer need to use their glasses.

GRIEF AND WORRY.

Similarly, an overload of mental strain makes individuals more susceptible to dental infection. Probably no contributing factor so greatly lowers the defense, unless it be an influenzal infection, as the mental condition in grief or anxiety. To illustrate:

A family of five girls nursed their father through a long illness, terminating in death from pernicious anemia, which was followed by a severe illness of the mother and final death from heart involvement. These girls were not physically exhausted from nursing duties, but were nearly prostrated by grief. All developed rheumatic group lesions such as neuritis, and two had heart involvements. The conditions were very markedly improved, and the neuritic symptoms relieved by the removal of dental infections.

An experiment was made to determine the effect of worry. Two ferrets were secured and put into a compartment within a rabbit's cage. At first the rabbits seemed very fearful of them but as soon as they learned that the ferrets could not hurt them, they entirely ignored their presence. Results of this test were negative.

EXPOSURE.

Physical exposure is probably one of the most serious and most common of the overloads which come upon the human body to lower its defense and make it a prey to the focal infections against which it has, under normal conditions, an ample defense. In Chapter 64 on acute rheumatism, I give the history of a case of a man who was a partial invalid from a form of neuritis for over twenty years, following exposure, repairing a burst water main in the winter, which threatened to do great damage to the factory in which it happened. This man worked in the nearly ice-cold water for about two hours repairing the break. At the time of this exposure, and for a year preceding, he was having dental work done, including the treating of several infected teeth. His neuritis was so severe that it drew his knees nearly to his chin for many weeks, and one arm was almost useless from atrophy.

To test this we have made cultures from the teeth of a patient suffering from rheumatism and have made inoculations into four rabbits, two of which were used as controls, kept in a warm cage, and received the same inoculations as the two being tested, which latter were submitted every day or two to exposure of cold, by having their hind legs immersed in water with broken ice in it. The dosage in these cases was purposely small. The control rabbits received twelve inoculations within a period of thirty-two days. The two exposed to the chilling received the same inoculations on the same days. All of the rabbits lost in weight following the inoculations. The average loss of weight of the two that were not exposed to the chilling was 10 per cent, and of the two that were exposed was 14 per cent. But this is not the most important effect of the exposure. The two that were not exposed did not develop any lesions from the inoculations. One is still living four

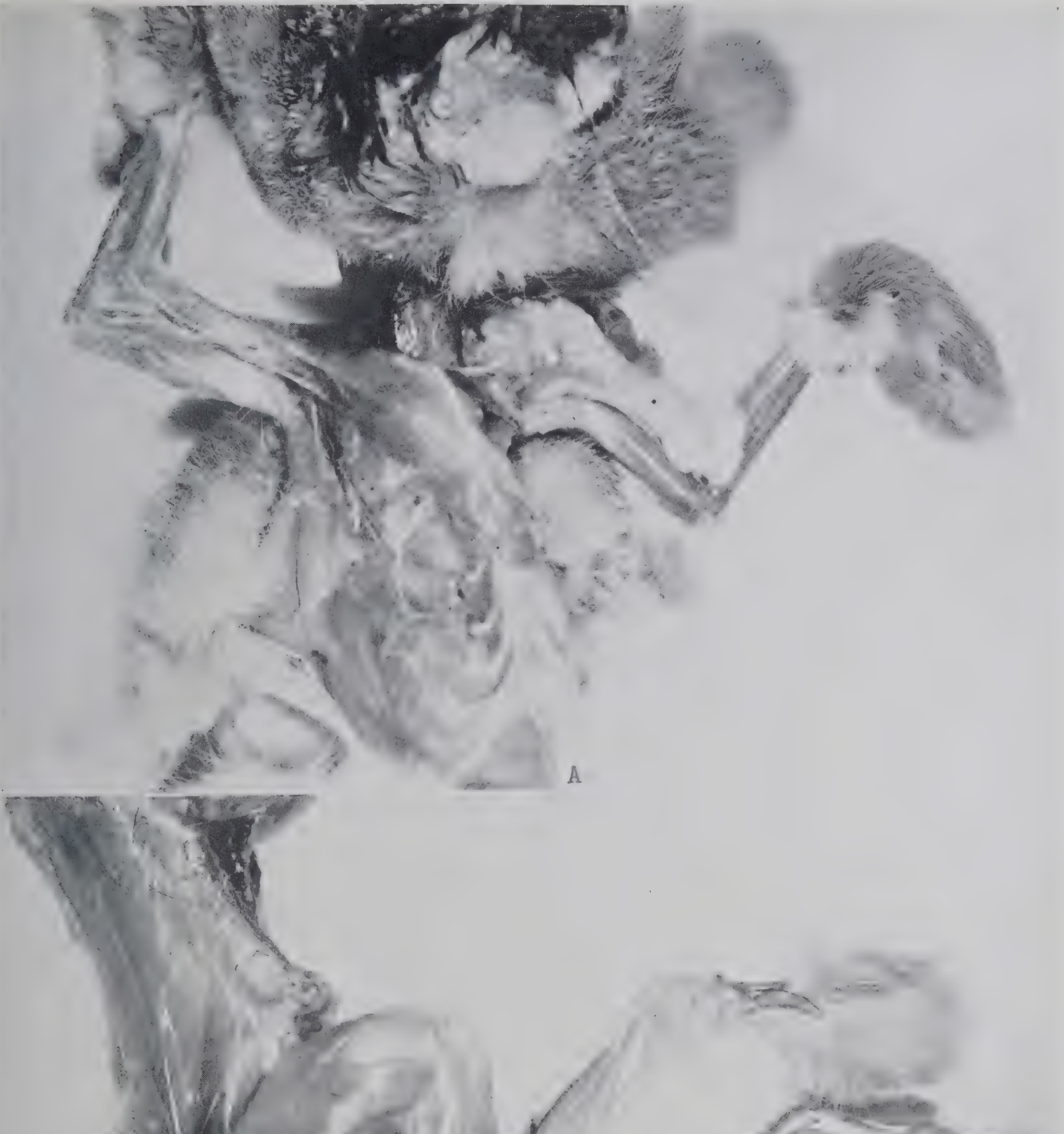

FIGURE 142. A AND B SHOW TWO RABBITS WHICH DEVELOPED ACUTE SUPPURATIVE ARTHRITIS FROM SMALL INJECTIONS OF DENTAL CULTURE, PLUS CHILLING IN COLD WATER. THE TWO CONTROLS RECEIVING THE SAME CULTURE BUT NOT CHILLED DEVELOPED NO LESIONS.

months after inoculation, has gained in weight to 241 grams. The other has recently been used for another experiment, it having gained considerably in weight following its last inoculation. The two that received the chilling, however, developed very severe rheumatic lesions, both of which are illustrated in Figure 142, A and B. A shows an extensive intracapsular abscess of the left shoulder, extending into the muscle sheath. B shows a subcutaneous multiple suppurative arthritis of the right shoulder and the left wrist and third and fourth digits.

We have here an illustration of what happens when an individual with an infected tooth is exposed to severe chilling. During the period of normal exposure he may have a loss in weight and some depression and injury, expressing itself chiefly as lassitude or marasmus, or both; but on exposure to cold or other depressant, the resistance of the tissue is seriously lowered, the total defense of the body goes down, and the rheumatic lesions appear, which may be rheumatism, neuritis, or functional disturbances of special organs, as was illustrated by the case of the man chilled in repairing the burst water main.

There is a phase of this problem of exposure which is very obscure and involved. We have all seen individuals who would remind us that their joints felt like rain, which seemed clearly to indicate, since they were so often correct, that their biological mechanisms were responding to changes of humidity and atmospheric pressure. Our researches recorded in the preceding chapters have strongly indicated that whatever other factors are largely variable, of which doubtless there are many, the ionic calcium is apparently very important. We have found, as shown in Chapter 20, that the presence of focal streptococcal infection tends to reduce the ionic calcium of the blood throughout the entire circulation, and very markedly so when the tooth is placed directly in the serum of freshly drawn blood for a couple of hours. If, then, these individuals have their ionic calcium reduced to, or nearly to, the threshold, we can readily understand that a local depression of some part of the body by chilling, might throw the calcium content below the threshold at that point. Accordingly, if the patient sits in a draft when he or she has an infected tooth, the circulation ionic calcium being near the threshold, that of the back of the neck where the draft strikes is sent below that point. That tissue, then, has lost, temporarily, its reserve defense; it is a prey to the toxic invasion passing through the system, and more or less severe symptoms from a mild myositis to a muscle spasm with torticollis are the result; or there may be neuritis of the cervical nerves. The problem of tissue temperature has also a very direct effect on susceptibility and defense.

Two things are most logical as a treatment: First, to remove the source of infection after it can be found, (not that all toxic irritations come from dental infections or even all from focal infections) and to raise the defense of this local tissue by both the application of heat and the liberation into the fluids of the involved tissue of ionic calcium through the process of massage. To test the first of these we have very many times, as recorded in subsequent chapters on the pathology of systemic dental infections, completely relieved these symptoms permanently or for years by the removal of dental foci, though they had been coming with very great frequency. To determine the form of different mechanisms that are operative in the process of massage of various types, we have made determinations of the ionic calcium of the blood in a given tissue, say a rabbit's ear, and then massaged the rabbit's ear first lightly and made determinations, then vigorously, and finally very vigorously, and have found that mechanical irritation of the tissue slightly changes the ionic calcium of the blood from that tissue.

It is a question whether the osteopaths will ever appreciate, and it is to be hoped the laity never will, how much that group is indebted to the dental profession for the preparation of a group of patients with an affection that will keep them coming; and we trust that the gratitude of the patients who have had these successive treatments made unnecessary, will adequately offset the curtailment of the visits to the physical therapists which will result from a final intelligent removal of dental foci.

In the chapter on sensitizations we discuss not only anaphylaxis as an antigen-antibody reaction, but also the phenomenon of local tissue sensitization, which it is probable are important factors in the development of this infinitely sensitive mechanism which makes it possible for the grandmothers and grandfathers and some not yet graduated into that class, to be such efficient weather prophets.

NUTRITION AND HUNGER.

Since every machine is dependent upon its supply of fuel if it is to maintain its output of energy, the human body is dependent upon the nature and quantity of its food supply. In the chapter on nutrition we discuss this definitely from that viewpoint, for few, if any, of the overloads of the human body will so often be found to be a contributing factor as will faulty nutrition. In this chapter we are discussing the relation of overloads to dental focal infections. There are, accordingly, two distinct methods by which this occurs. The individual who is hungry is more susceptible to infection of any kind. For years it has been the teaching, in medicine, that no man should go into the presence of contagion, hungry or with an empty stomach, because his defense would be lowered. The reasons for this are most apparent. Without an adequate fuel in the furnace, the generation of heat is diminished and the temperature of the dwelling decreases. The chemical processes of the body are practically all increased with an increase of temperature, with each increase of which, above normal, the reactions of the body are increased approximately ten per cent; and, similarly, with each decrease of which, the reactions are reduced approximately a similar amount. This is a fundamental factor in the problem of exposure to which we referred in a previous paragraph.

But there is another important method by which nutrition directly acts upon the process of defense. Metabolic processes, and particularly calcium metabolism, are dependent upon certain chemical substances, the nature of which we do not yet understand, which are derived from various glandular tissues of the body, generally referred to as the glands of internal secretion, and upon certain substances spoken of as accessory food factors or vitamines, a certain quantity of which will be necessary for metabolic and catabolic processes. The quantity factor of these is, incidentally, small and is discussed in the chapter on nutrition.

EXHAUSTION, PHYSICAL AND NERVOUS.

It has long been said that work never kills but worry does. It is exceedingly difficult to determine what are the chief factors involved in exhaustion, partial or complete; that is, whether the fatigue is chiefly a quality of the musculature or of the nervous system. Our clinical experience reveals many cases where partial exhaustion, or long continued overload of work, seems to contribute very directly to increasing the susceptibility to focal infections. It is exceedingly difficult in any clinical case to eliminate such factors as worry, lack of nutrition, exposure, etc. Because of this difficulty to exclude all other contributing factors, it seems unsafe to quote clinical cases.

ACUTE AND CHRONIC INFECTIONS.

It seems probable that any disturbance, whether physical or infectious, tends to disturb the normal defensive factors of the body. A very common overload of an infectious nature, but fortunately much less common than previously, is typhoid fever. We find in our case histories that many patients have their first attack of acute or chronic rheumatism accompanying or following typhoid fever. To what extent these patients would have been involved had they not had focal streptococcal infection is, of course, impossible to state. The following seems to be a typical history of some of these cases.

About thirty years ago this patient had typhoid fever at the age of about twenty. Immediately following her typhoid, she developed acute rheumatism with progressive arthritis deformans. I have watched her case for twenty-eight years, during most of which time it became progressively worse until she was entirely unable to walk. I sent for her six years ago in order that I might remove some teeth that I had crowned twenty years previously. The removal of these dental infections not only prevented the condition from becoming progressively worse, as it had been advancing, but since that time it has become progressively better. It seems very probable that the acute onset was largely due to her broken defense, and its attending disturbances of nutrition, etc., occasioned by her typhoid infection.

SYPHILIS.

In discussing the role of another infection as being contributory, the matter becomes much more complicated when we consider an organism which, of itself, is able to produce lesions which may be comparable to those produced by the injected streptococci. It is, however, a frequent observation that patients presenting with involvements of the nervous system and at the same time carrying a dental focal infection, seem to be more susceptible to their dental infections than normal.

The two types of nerve reactions are sufficiently different to be differentiated, even when present at the same time in the same patient. The streptococcal involvements are acute and recessive, the recurrences and exacerbations being characteristic in that they are relieved by salicylates, and are improved by massage. On the contrary, the syphilitic disturbances are more persistent and continuously progressive without the marked exacerbations and recessions that accompany streptococcal involvements. The removal of the dental foci will often relieve permanently these typical rheumatic type disturbances, while the less variable and progressive symptoms of the syphilitic infection will not be relieved by the removal of the dental foci. In a later communication I will discuss the means for differentiating, and the frequency of the presentation of lesions, which are thought to be rheumatic of streptococcal origin, but prove to be syphilitic processes. In a later communication I will discuss the need for careful differential diagnosis between streptococcal focal infection reactions as rheumatism, particularly of the knees, and rheumatic disturbances of very similar nature of gonorrheal origin.

ALCOHOL.

It is not strange that alcoholics are more susceptible to streptococcal infection from focal dental infection or other source than normal. Any substance which, when taken into the system, disturbs cell function would be expected to disturb defense. This is a very common clinical experience.

SUMMARY AND CONCLUSIONS.

The individuals constituting the members of the group we have designated as having an acquired susceptibility, have in large part come into that group as the result of overloads plus focal infection. It is probably not fair to speak of old age as an overload. It is, however, true that much less increase above normal constitutes a potential overload for the aged than the middle-aged; and, similarly, of the middle-aged than over the vigorous young.

The overload that we have most frequently found to have been the cause of transferring an individual from the group of absent susceptibility to acquired susceptibility is influenza. And in this connection it is significant that statistics that have been accumulated in England and Wales have shown that in the two years following the epidemic of Flu, approximately four times as many individuals died from the complications following and incidental to Flu as did from the Flu attacks. Our own studies have also shown that the prevalence of grave complications with influenza is two and one-third times as great in the group of individuals having dental infections, as in the group free from dental infections. It now seems evident from these and our inoculations on animals, that focal dental infections are a potential danger, because of the complications arising from them incidental to an attack of Flu, of far greater seriousness and importance than has been realized. Such an individual is carrying a potential charge of dynamite which may, when least expected, explode and involve his system and gravely endanger his life, for, of the individuals with complications whom we have found in the hospitals, thirty to fifty per cent died.

We have alluded to the fact that, whereas the percentage of males and females in the group which we designate as non-susceptible, is approximately equal, the percentage of females to males rapidly increases in direct proportion to the severity of the susceptibility, changing from fifty-fifty in the absent susceptibility to ninety-three per cent of females in the strongly inherited group to seven per cent of males. Our studies have shown that this change in ratio is largely the result of the increase of overloads induced by motherhood. Pregnancy is, therefore, one of the most important overloads which must be reckoned with, and prepared for, to which the human body can be subjected.

Similarly, overload of tissues such as physical injury, extreme anxiety, exposure, nutrition and hunger, exhaustion, physical and nervous, acute and chronic infections, syphilis, and alcohol, all contribute singly or collectively to breaking an otherwise ample defense. The individual without the dental infection, would suffer depression or exhaustion, from which he would readily recover, but with the presence of focal infection, finds himself the victim of an enemy he does not recognize and cannot reach. He breaks in some of the special tissues, frequently the one that has been overloaded or exposed. The tendency has been to treat the symptom, and it has often taken long periods of time for the patient with forced rest and every effort to reduce the overloads, to regain the mastery of his focal infection. Our clinical experience is that scores of these people go right on with their overloads, with complete relief from their physical symptoms due to the infections, when the dental infections or other focal infections are removed, showing clearly that the primary disturbance has been the infection. The individual has proved to have ample strength to carry his normal physical burden if relieved of his focal dental infection, which latter will often be sapping his system of more of his vitality and nerve energy than will his entire physical and nervous energy combined.

We would briefly summarize by saying that the individual with an absent susceptibility to rheumatic group lesions, is in a condition of only relative safety, for at any moment that his overloads of age, physical and nervous expenditure, exposure and grief, contributing infections, shall singly or in combination lower his total defense, he will become a prey to that dental infection which will attack his weakest link, which in these cases of an acquired susceptibility, whether in part or in combination with a mild heredity, will tend to be the most susceptible tissue, and most frequently the nervous system.

> **Dental infections, while potentially harmful, may not be causing apparent or serious injury until the individual is subjected to some other overload, at which time a serious break may come. The chief contributing overloads are influenza, pregnancy, lactation, malnutrition, exposure, grief, worry, fear, heredity, and age.**

CHAPTER XXII.

ELECTIVE LOCALIZATION AND TISSUE AND ORGAN SUSCEPTIBILITY PHENOMENA.

PROBLEM: Do the organisms of dental infections possess or acquire tissue affinity and elective localization qualities?

EXPERIMENTAL AND DISCUSSION.

Seldom in the history of any problem in medicine has the storm centered around a single individual as it has, in this instance, around the pioneer worker and chief advocate of elective localization on the part of streptococci, Dr. E. C. Rosenow; and few, if any, of the contributions to medicine of the last two decades are likely to promise so great helpfulness to humanity, as the development of the relationships of focal infections to the degenerative diseases. The antagonism and opposition have grown out of a lack of knowledge of the mechanisms constituting the attacking forces of the invading organisms, and of the defensive forces of the hosts. (The bibliography of this discussion would cover hundreds of pages of references and would not be necessary or appropriate here.)

Probably no problem in connection with this most complicated group of pathological processes is so complicated and so certain to be misunderstood by many who read as will this phase. To many people there will be little difference at first thought between elective localization, and organ and tissue susceptibility, notwithstanding they are very different, since the former pertains to qualities which relate exclusively to the bacterium, and the latter to qualities which relate exclusively to the invaded special tissues. These are so distinct that they should be discussed in two separate chapters. Yet we have combined them in order to emphasize the need for their differentiation by specific reference made continually through this discussion.

There is another reason why the discussion of this subject is unusually difficult: namely, the prejudice amounting to almost unalterable convictions in two groups, one of which has maintained, that elective localizations should not be anticipated because of evidence developing from experimental data. Some of the disbelievers have tried and it did not work; therefore, it is not so.

A review of the elective localizations resulting from inoculation of a thousand rabbits with cultures taken from dental infections of various types, with and without acute processes on the part of the patient, but generally with, should, according to the claims of the extremists, prove or disprove whether it is possible for bacteria to carry into animals an elective localization quality corresponding with the lesion of the host from whom the tooth was extracted.

A study of any successive thousand inoculations would necessarily include so many different varieties of problems that the data would not all be directly related to this particular phase of elective localization. Instead, then, of making our specific studies of the quality of elective localization as an inherent property of the microbe, we have taken groups of inoculations from individuals with, and without acute processes in various tissues of their bodies, and in whose cases the organisms had been taken from the teeth, and after culturing by comparable methods had been inoculated in comparable doses into animals by comparable methods. Results of these studies and comparisons are more instructive than could be a miscellaneous group of inoculations made under dissimilar conditions and by methods that were not comparable.

In the first place, this group of experiments includes all types of studies, many of which were not even indirectly related to discovering the qualities implied in elective localization. In fact it includes, in many cases, experiments made to demonstrate that elective localization would not take place under the conditions of the experiment. There are so many factors involved which, as yet, even those best informed from intensive study do not understand, that no group of figures can be considered conclusive. To illustrate:

Few animals were considered more susceptible or more certain of death from inoculation of the anthrax bacillus than the guinea-pig; and, yet, it is now demonstrated by Besredka and Noetzel[12] that, if the guinea-pig could exist without its skin, it would be entirely immune to anthrax; that it can be injected with lethal doses into the blood stream or peritoneal cavity without serious injury, but the most extreme care must be taken, not to permit one organism to reach the skin. If, then, two experimenters undertake to test whether or not the anthrax organism will kill guinea-pigs, without a knowledge of this fact, one individual may prove conclusively that the animal is immune because his technic is actually different, though apparently the same, in the matter of contamination of the skin with the organism in the process of inoculation.

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[12] See bibliography.

The attitude of mind on this question can be illustrated by the following experience of the writer. I received a letter from a man in another state, stating that he was sending, under separate cover, some teeth that he had extracted from a patient, and that he desired to test whether or not there was any truth in the theory of elective localization by having me inoculate rabbits and develop in them the lesions, and report the lesions to him; and, if they were the same as those suffered by his patient, of which, of course, I was not informed, he would believe in the theory; and, if not, it would be proof to the profession that there was no truth in the theory. The teeth arrived after many days in a dry condition in a pasteboard box, overgrown with a mold, probably contamination. Of course, this is not comparable to that of the just critics of elective localization; and we have desired to keep ourselves free from opinion and prejudice for either side of the argument in conducting these studies.

The following experiment was made to throw light upon the question of the influence of the culture medium upon the quality of elective localization, if such resided in the organism. A culture was made from the live but infected pulp of a tooth of a boy nine years old who was suffering from an acute endocarditis and acute rheumatism with very severe symptoms. Thirty rabbits were inoculated in the first group with the culture grown out in ascites broth, 24 hour growth, centrifuged, washed, and inoculated in normal salt solution. One hundred per cent of the rabbits developed acute rheumatism, and 93 per cent acute heart involvements. The same organism was grown on artificial media for seventeen days, when another group of animals was inoculated, only 10 per cent of which developed heart lesions. All other conditions were as nearly constant as we could maintain them.

On inquiry of men who have stated that they had succeeded in developing evidence of elective localizations, and of others who have similarly experimented, but have not developed localiza-

SUMMARY OF ANIMAL REACTIONS AND PATIENTS' SYMPTOMS

Case Number	Patients' Chief Lesions	No. of Rabbits	Percentage with Major Lesions	Heart	Lungs	Liver	Gall-Bladder	Stomach	Intestines	Appendix	Kidneys	Urinary Bladder	Generative Organs	Joints	Muscles	ands	Spinal Cord	Brain	Eyes	Rheumatism Clinical	Chloroform
1124	Pelvic Inflammation and Discharge. Neur.	7	**100**	43	14	14			14		14		**28**	**57**	**14**	14				**14**	86
1087	Eyes. Nervous System	11	**100**	9	9	27	9		9	9	9			9	18		9		**100**		82
1094	Acute Rheumatism	12	**42**	33	8	33	8		33	8	33			**25**	**16**					**16**	75
1095	Heart. Rheumatism	2	**100**	**100**	100	50	50		50		100				**50**			50		**100**	0
306	Rheumatism	3	**33**	33									33		**33**					**33**	100
1098	Lassitude	6	**67**	67	33	33	17	17	33		50				50						50
381	Arthritis	2	**50**			50								**50**	**50**					**50**	50
1081	Neck and Shoulder Inv.	5	**40**	80		40			20	20	40		20		**20**	20	20	20		**40**	20
1085	Ovarian Pain	6	**67T** **100F**	33		83	17		67	17	50	33	**67T** **100F**								50
1050	Rheumatism. Heart. Uterine Pain and Discharge	13	**55**	**23**		31	8		8				**8**							**8**	**85**
1065	Lumbago. Myositis	3	**100**	67	33	100	33		67		67			**33**	**33**	33				**100**	33
581	Heart. Rheumatism	6	**100**	**100**	17	67	33	17	33	17	50			**33**	**50**					**50**	**67**
1049	Mild Rheumatism	4	0																		**100**
1057	Heart. Rheumatism. Emacia	6	**83**	**50**		33	33				17				**17**	17				**33**	67
1014	Neuritis. Myositis	10	**20**	30		80	50		60	20	30				**10**					**20**	30
1058	Heart	3	**100**	**100**	33	100		33	33		100			100	33					67	33
311	Heart. Rheumatism	2	**100**	**100**	50						50			**50**	**50**						50
1009	Heart. Arthritis	5	**100**	**100**		60			20		60				**20**				20	**40**	40
1048	Neuritis. Gall Stones	5	**100**		20	40	**40**	20	20	20	20				**20**	20	20	20	20	**60**	80
709	Arthritis	4	**100**	25		50	25		25		50			**50**	**50**	50		25	50	**100**	75
455	Rheumatism	9	**78**	22		11								**22**		11				**78**	100
1008	Eyes	13	**62**	38	8	54	31	23	69	15	54	8	15	23	31		8	8	**62**	8	23
1019	Diarrhea. Lameness in Shoulder and Arm	4	**100**			75	50	25	**100**			25			**25**	50				**75**	100
1005	Rheumatism	3	**100**																	100	100
987	Eyes. Rheumatism	12	**83**	58	25	42					33	33	25	33	25	17		8	**58**	**50**	58
955	Xerostomia. Rheumatism	12	**83**	33	42	33					33	8	8	**17**	**8**	**83**				**8**	67
1024	Rheumatism	10	**60**	30	30	30		20			40			**20**	**30**	10				**50**	60
433	Rheumatism	2	**50**	100	50	50		50			100			**50**	**50**	50				**50**	0
433	None	2	**None**																		100
938	None	4	**None**																		100
	None	1	**None**																		100

FIGURE 143.

tions, we have found many instances where it seemed that the explanation might be found in the methods of procedure, including the length of time the organisms had grown on artificial medium and the nature of that medium. For example, some men plate out the organisms on Petri dishes, pick off a colony in 24 or 48 hours, plate it on another Petri dish and when it has grown sufficiently to plant others, transfer again until finally enough dishes are covered, from which to wash the organisms for inoculation, which may take several days. In some cases, with which we are familiar, the organisms were grown in artificial media for five days, and in other cases as long as seven days. This is so important a factor, that it might well be used as an experiment to determine whether or not growing the organisms on artificial media, would efficiently eliminate elective localization qualities, if they existed.

In studying our large groups of inoculations, we find very distinct evidence that some types of lesions produce very large percentages of localizations whereas others do not. We have also found that different types of the same lesion will produce in some instances very large percentages of localizations, while others will produce a low percentage. In Figure 143 we show the result of inoculating 187 rabbits with cultures from the teeth of thirty different patients. This group represents a quite large variety of conditions, some acute, some chronic, some without lesions. The result of this study has shown that, in a large number of instances where the process was an acute one, the method of inoculation used showed evidence of elective localization in a high percentage of cases, often 100 per cent; that where the process was a subacute or chronic one, it was often a low percentage of localization; and when there was no lesion, there was often a very indefinite expression in the rabbits or no expression. (See the last three.)

There are many factors involved which modify the final results as, for example, the relation of the size of the dose to the weight of the animal. Many experiments are recorded in these various studies which illustrate this, though this mass action relation has not always been the purpose of the experiment. A splendid illustration of this phenomenon is shown in Figure 144 by inoculating three rabbits, Nos. 571, 572, and 573, with the same quantity of the same strain. All three were inoculated intravenously September 13 with 1 cc. of culture from four incisors, grown out 24 hrs. in plain broth; organisms washed and suspended in sodium

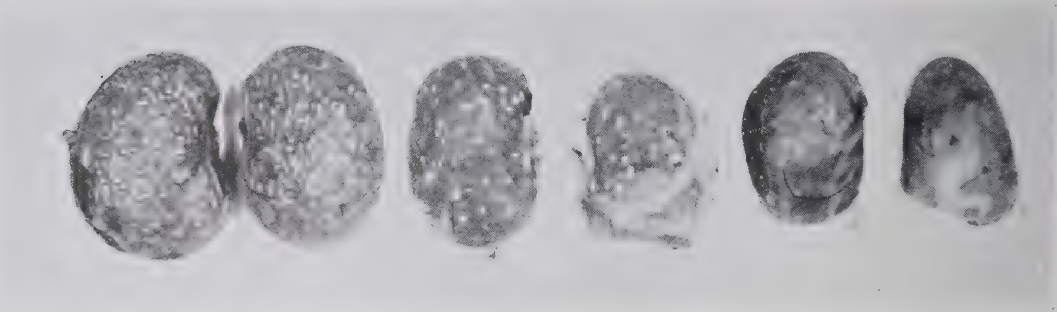

FIGURE 144. MULTIPLE KIDNEY ABSCESSES PRODUCED IN THREE RABBITS. ALL RECEIVED THE SAME CULTURE AND THE SAME TIME FACTORS. RESULTS ARE INVERSELY WITH THE WEIGHTS OF THE RABBITS.

chloride solution; three billion to 1 cc. All were chloroformed September 19. Since all were posted after the same length of time the results are comparable. This culture had a marked affinity for kidney tissue, and the figure shows the three pairs of kidneys from these rabbits, mottled with multiple abscesses; the smallest rabbit almost completely covered with abscesses; the next larger, many less; and the largest rabbit, relatively only a few visible on the surfaces; yet the elective localization was clear in them all.

This quality of elective localization is an exceedingly variable one. In some cases large percentages of the rabbits will have principally or exclusively one lesion, which may or may not be the lesion from which that individual is suffering at the time. This is illustrated in the chart in Figure No. 145 in an analysis of the lesions of the different rabbits inoculated with the cultures from a series of patients with involvements of joints and muscles. We could pick many dozens of cases, if we simply wished to present positive evidence, in which from 75 to 100 per cent of the rabbits had developed joint and muscle involvements. This group is selected to show that it is not always so.

The first patient was suffering from an arthritis, acute and chronic. Four rabbits were inoculated. All developed acute rheumatism; but in addition, one developed heart, two liver, one gall-bladder, one intestines, two kidneys, and one had a brain lesion.

The second patient suffered acutely from rheumatism. Nine rabbits were inoculated. Seven rabbits developed acute rheumatism; one developed liver involvement, and two heart. A striking thing about this series was, that every rabbit was chloroformed after it had developed acute lameness, such as carrying its leg,

JOINTS AND MUSCLES

R. No.	Material	Date Injected	Date of Death	Case No. and Lesions	Percentage with Major Lesions	Heart	Lungs	Liver	Gall-bladder	Stomach	Intestines	Appendix	Kidneys	Urinary bladder	Generative organs	Joints	Muscles	Rheumatism Clinical	Nerve trunks	Spinal cord	Brain	Eyes	Chloroform
194	C	2–18	2–22	709	100			x	x		x		x				x*	x*			x	?	x
196	C	2–18	3–2	Arthritis,				x					x			x*	x*	x*				?	
215	C	3–5	5–2	acute and		x												x*					x
217	C	3–5	5–2	chronic												x*		x*					x
				4 Rabbits		25	0	50	25	0	25	0	50	0	0	50	50	100	0	0	25		75
182	C	2–11	5–2	455	78			x										x*					x
183	C	2–11	3–15	Rheumatism												x*		x*					x
185	C	2–11	2–27															x*					x
186	C	2–11	3–9															x*					x
192	C	2–16	3–9															x*					x
195	C	2–16	2–18			x																	x
202	C	2–18	5–2																				
345	C	5–9	6–17															x*					x
346	C	5–9	6–17													x*		x*					x
						x																	x
				9 Rabbits		22	0	11	0	0	0	0	0	0	0	22	0	78	0	0	0	0	100
				1065	100			x									x*	x*					x
257	C	3–24	3–25	Myositis.																			
260	C	3–24	4–17	Neuritis		x		x	x		x		x			x*		x*					
262	C	3–25	4–15	Lumbago		x	x	x			x		x					x*					
				3 Rabbits		67	33	100	33	0	67	0	67	0	0	33	33	100	0	0	0	0	33
				1065	0	x																	x
416	W	6–14	7–13	Myositis.				x															
423	C	6–15	7–13	Neuritis				x															x
424	C	6–15	6–23	Lumbago				x															
				3 Rabbits		33	0	100	0		0	0	0	0	0	0	0	0	0	0	0	0	67
184	W	2–18	3–2	1024	60		x	x		x													
199	C	2–22	2–28	Rheumatism		x	x									x*	x*	x*					x
203	C	2–24	3–1			x	x	x		x							x*	x*					x
216	C	3–5	3–28																				x
218	C	3–5	3–28													x*		x*					x
219	W	3–7	3–21			x							x					x*					
221	C	3–8	3–28										x										x
222	C	3–8	3–28															x*					x
343	C	5–6	5–22					x					x				x*						
344	C	5–6	5–7										x										
				10 Rabbits		30	30	30	0	20	0	0	40	0	0	20	30	50	0	0	0	0	60
				Average	68	35	13	58	12	4	18	0	31	0	0	25	23	66	0	0	5	0	67

FIGURE 145.

which process subsided; and at the time of the postmortem, in only two of these rabbits was there still evidence of the lesion which had expressed itself so acutely, usually about two days after inoculation. In the previous case of the four rabbits developing acute rheumatism, only two showed involvement of the joints at the time of postmortem, and two involvements of the muscles. In the fourth one the involved tissue had apparently entirely recovered.

The next two cases are the same patient at two different times. Her disturbance was recorded as myositis, neuritis, and lumbago. At the time of the inoculation of the first group of rabbits, all three developed acute rheumatism; but, in addition, two developed heart, one lung, three liver, one gall-bladder, two intestines, and two kidney. Later, after her acute process had subsided, another group of rabbits was inoculated with the culture from another tooth, at which time none developed rheumatism, all three developed liver involvement, and that acutely; and with the exception of one rabbit which had a severe heart lesion, there were no other lesions in any of the three rabbits. Note that in both series of inoculations from this patient all of the rabbits developed lesions of the liver, which lesion appeared in only one rabbit out of nine in the preceding case.

In the last case the patient suffered from acute rheumatism. Ten rabbits were inoculated. Five of the ten developed clinical rheumatism and one myositis, making six rabbits with joint and muscle involvement. Three had heart involvement, three lungs, three liver, two with stomach, and four with kidney involvements. These rabbits were inoculated with the culture from the teeth at the time the patient was having acute rheumatism and from which she had been suffering severely for some time. Incidentally, she has not had a recurrence of the disturbance since the removal of the infected teeth three years ago.

In this case the first and sixth rabbit in the list were inoculated with washing from the teeth, followed by a culture from the teeth two weeks later. This will be discussed again under anaphylaxis. The effect of the previous injection with the filtered washing was to make these rabbits much more sensitive to the culture grown from those teeth. One of these rabbits died three hours following this injection, notwithstanding the fact that it was the first time organisms had been injected into this rabbit, and the dose was not large enough to produce serious or immediate disturbance. The other died on the second day.

EYES

Rabbit No.	Material	Date Injected	Date of Death	Case No. and Lesions	Case No.	Percentage With Major Lesions	Heart	Lungs	Liver	Gall Bladder	Stomach	Intestines	Appendix	Kidney	Urinary Bladder	Generative Organs	Joints	Muscles	Rheumatism Clinical	Nerve Trunks	Spinal Cord	Brain	Eyes	Chloroform
169	W	1–10	2–24	1008	1008	62						x			x								x*	
173	W	1–12	6–10	Eyes															x				x*	x
174	C	1–13	4–15									x							x				x*	
207	W	2–24	3–10																				x*	
209	W	2–24	3–14						x			x		x				x					x*	x
263	C	3–30	3–31				x		x		x	x		x										
264	C	3–30	4–21				x	x	x	x		x	x	x		x							x*	
267	C	3–31	3–31				x		x		x	x		x										
276	C	4–4	4 27						x	x		x	x	x				x						
287	W	4–12	6–6				x										x	x						
290	W	4–12	4 27						x	x	x	x		x		x		x	x		x	x		
296	C	4–13	5 11				x		x	x		x		x			x						x*	
298	C	4–13	6–8														x						x*	x
				13 Rabbits			38	8	54	31	23	69	15	54	8	15	23	31	23	0	8	8	62	23
369	C	5–15	6–25	1087	1087	100	x		x								x						x*	x
371	C	5–15	5–25	Eyes				x	x	x		x	x	x				x					x*	
374	C	5–15	7–6	Nervous system.																			x*	x
375	C	5–15	6–23	Mental Cloud																			x*	x
383	C	5–24	6–23																				x*	x
384	C	5–24	6–6																				x*	
402	C	6–7	7–6																				x*	x
403	C	6–7	7–6																				x*	x
410	C	6–14	7–13																				x*	x
418	C	6–14	7–1						x									x			x*		x*	x
419	C	6–15	7–13																				x*	x
				11 Rabbits			9	9	27	9	0	9	9	9	0	0	9	18	0	0	9	0	100	82
143	C	12-28	1–5	987	987	83	x	x	x														x*	
151	C	1–3	1 16	Eyes			x	x	x					x	x	x								
155	C	1–5	4 22	Rheumatism												x	x*		x*				x*	
156	C	1–5	1 5											x										
157	C	1–5	1–18				x							x					x*					x
158	C	1–4	6–20														x*							x
160	C	1–7	1–18				x		x						x				x*					x
161	C	1–7	2–19						x									x*	x*				x*	
162	C	1–7	2–26					x	x									x*	x*			x	x*	x
163	C	1–7	1–14				x																x*	x
164	C	1–7	1 20				x							x	x	x	x*	x*	x*				x*	x
165	C	1–7	1–19				x								x		x*						x*	x
				12 Rabbits			58	25	42	0	0	0	0	33	33	25	33	25	50	0	0	8	58	58
				Average		82	35	14	41	13	8	26	8	32	14	13	22	25	24	0	6	5	73	54

FIGURE 146.

Few tissues have shown a higher percentage of localization than eyes when the process is an acute one. It does seem necessary, however, that the culture be taken from the tooth at a time when the patient's eye is in a state of acute reaction. This is illustrated in Figure 146 on Eyes, which shows three cases.

In the first, thirteen rabbits were inoculated from the cultures of the teeth of a patient with two types of lesions of the eyes: exophthalmos and extreme pain from the rupturing of blood vessels. This case is shown in Chapters 65 and 66. Of the thirteen rabbits 62 per cent showed eye involvement, 69 per cent showed intestines and digestive tract involvement, and many other severe lesions are recorded.

In the next case, eleven rabbits were inoculated and all developed acute eye involvements. This patient was almost totally blind in one eye and about four-fifths blind in the remaining eye. Note: With the exception of one rabbit which developed multiple lesions, most of the other rabbits developed only eye involvement.

The next patient had acute recurring involvement of both eyes, as part of a blood stream infection complication. Of the twelve rabbits, seven or 58 per cent developed eye involvements; 50 per cent developed rheumatism, from which the patient was suffering severely, and 58 per cent developed heart involvement, from which the patient also suffered.

A group of inoculations selected from patients with acute digestive tract disturbance, shown in Figure 147, will illustrate the variableness of this quality of elective localization of the organism growing in the teeth, where the patient is suffering from acute or chronic processes.

In the first case four rabbits were inoculated and all four developed acute intestinal involvement. The patient suffered from a diarrhea with movements every fifteen minutes. All of these rabbits developed diarrhea with this strain. All four were acutely involved.

In the next case the patient suffered from acute digestive tract disturbance. Of the six rabbits, three developed involvement of the stomach and intestines, one also of the gall-bladder and liver.

An effort was made to extract a toxin by passing the cultures in their media through Berkefeld filters. The filtrate, bacteria-free, was inoculated, and produced in nine rabbits, or 44 per cent, in-

DIGESTIVE TRACT

R. No.	Material	Date Injected	Date of Death	Case No. and Lesions	Case No	Percentage with Major Lesions	Heart	Lungs	Liver	Gall-bladder	Stomach	Intestines	Appendix	Kidneys	Urinary Bladder	Generative Organs	Joints	Muscles	Rheumatism Clinical	Nerve Trunks	Spinal Cord	Brain	Eyes	Lassitude	Chloroform
187	A	2–15	2–21	1019	1019	100			x			x*			x			x*	x*						x
189	C	2–16	3–28	Diarrhea. Lame-					x	x		x*							x*					x*	x
190	C	2–16	3–28	ness in right																					x
200	A	2–22	2–28	shoulder and					x	x	x	x*							x*					x*	x
				arm. Lassitude								x*												x*	
				4 Rabbits			0	0	75	50	25	100	0	0	25	0	0	25	75	0	0	0	0	75	100
319	A	4–28	6–9	1098	1098	83																		x*	x
341	A	5–9	5–26	Digestive tract			x	x	x*	x*		x*		x				x						x*	
347	A	5–9	6–9	Lassitude			x					x*		x				x						x*	x
349	A	5–9	5–17				x	x	x*		x*			x											
362	C	5–11	6–9				x											x						x*	x
363	C	5–11	5–21																						
				6 Rabbits			67	33	33	17	17	33	0	50	0	0	0	50	0	0	0	0	0	67	50
231		3–16	3–29	Stock Toxin					x			x													
232		3–16	3–17																						x
233		3–16	3 22				x											x						x	x
239		3- 18	6- 24																x					x	x
240		3–18	4–3				x		x			x		x					x					x	
252		3–23	4–1						x	x				x				x	x						
253		3–23	5–8				x		x			x												x	
254		3–23	4–1						x	x				x				x						x	
255		3–23	4–4						x			x		x											
				9 Rabbits			33	0	67	22	0	44	0	44	0	0	0	33	33	0	0	0	0	56	33
229	W	3–15	5–13	1057	1057	83																			x
241	C	3–18	5–13	Digestive Tract															x*					x	x
243	C	3–18	5–13	Heart. Rheuma-																					
				tism															x*					x	x
256	W	3–28	4–15	Acidosis			x*																		
259	C	3–29	4–10				x*		x*	x*				x				x*						x	
261	C	3–29	4–6				x*		x*	x*															x
				6 Rabbits			50	0	33	33	0	0	0	17	0	0	0	17	33	0	0	0	0	50	67
				Average			38	8	52	31	11	44	0	28	6	0	0	31	37	0	0	0	0	62	63

C Culture
A Aspiration from cyst
W Washing

FIGURE 147.

testinal disturbances, liver involvements in 67 per cent, heart 33 per cent. This is discussed in detail in another chapter.

In the last case the patient suffered from a very acute digestive tract disturbance. Six rabbits were inoculated. None developed lesions in either stomach or intestines, three developed lesions in heart, two in liver, two in gall-bladder, three myositis and clinical rheumatism. This patient's primary condition was an acidosis, of which he died subsequently, but which had been apparently overlooked in his previous symptomatic treatment. His digestive disturbance, like several of his other expressions, was entirely secondary.

An analysis of one thousand rabbits, inoculated with cultures from dental sources of various patients, reveals some very interesting data in relation to the generative organs, as shown in Figure 148. It is very striking that in this large number of rabbits, approximately half of each sex, exceedingly few instances of involvement of the ovaries, tubes, and uterus of females, or testicles of males, have occurred where the patient from whom the culture was taken did not have acute infection or evidence of pathological condition of the generative organs.

The first and third cases in this chart are the same individual whose case is described in Chapter 62. In the first group of six rabbits there were four females and two males. This patient was suffering from ovarian disturbance so acute that she was kept in bed nearly a week at the time of her periods and suffered exceedingly. She had been struck over her ovary in playing golf some years previously, since which time, she had always had severe distress at the time of periods. The four female rabbits all developed acute infection of the ovaries and tubes, as illustrated in the chapter referred to above. The two males showed no involvement of the generative organs. At the time of her first involvement, some seriously involved teeth were extracted, and a root resection was made of a central incisor, with the hope that it might be saved or made safe until the end of her college year. Her trouble, which had been relieved by the removal of the dental infections on the first occasion, recurred. This questionable tooth which had been resected was removed; the culture inoculated into three female rabbits, two of which developed acute infection of the ovaries and tubes. Incidentally, she has not had a moment's return of her trouble since the removal of the last of these infected teeth.

GENERATIVE ORGANS

R. No.	Material	Date Injected	Date of Death	Case No. and Lesions	Case No.	Percentage with Major Lesions	Heart	Lungs	Liver	Gall-bladder	Stomach	Intestines	Appendix	Kidneys	Urinary bladder	Generative organs	Joints	Muscles	Clinical Rheumatism	Nerve trunks	Spinal cord	Brain	Eyes	Lassitude	Chloroform
277	C	4–6	4–28	1085	1085	100F																			x
280	W	4–5	5–4	Ovarian Pain		67T			x				x	x	x	x*									x
282	C	4–6	4–26	Headache			x		x			x		x	x	x*									x
283	C	4–6	4–19	Backache					x			x				x*									
335	C	5–5	5–16	Lassitude			x		x			x				x*								x*	
339	C	5–6	5–9						x	x		x		x											
				6 Rabbits			33	0	83	17	0	67	17	50	33	67	0	0	0	0	0	0	0	17	50
337	C	5–6	6–14	1124	1124	100										x*									x
409	C	6–22	6–24	Pelvic inflamma-															x*						x
432	W	6–21	7–14	tion and dis-																				x*	x
433	W	6–21	7–4	charge. Neuritis			x	x				x		x			x*								
440	C	6–22	6–25	Rheumatism			x									x*	x*								x
441	C	6–22	7–14	Lassitude					x								x*	x*							x
442	C	6–22	7–14	Headache			x										x*							x*	x
				7 Rabbits			43	14	14	0	0	14	0	14	0	28	57	14	14	0	0	0	0	28	86
506	C	7–29	8–2	1085	1085	67			x															x*	x
507	C	7–29	8–2	Ovarian pain												x*								x*	x
508	C	7–29	8–2	Lassitude												x*									
				3 Rabbits			0	0	33	0	0	0	0	0	0	67	0	0	0	0	0	0	0	67	67
				Average		89	25	5	43	6	0	27	6	21	11	54	19	5	5	0	0	0	0	37	68

x—Rabbit
*—Patient

FIGURE 148.

When patients are suffering from endocarditis in its acute form, cultures from the infected teeth tend to reproduce heart involvements in animals in a very high percentage. This is illustrated in Figure 149 on hearts. In the first patient shown, five rabbits were inoculated, all developing acute heart involvement. In the second case, that of a child bedridden with acute endocarditis, three rabbits were inoculated with culture from a deciduous tooth. All three developed acute heart involvements. In the third case the patient was a woman between thirty and forty years of age with acute heart involvement and dyspnea. Six rabbits were inoculated. All developed acute heart involvement. In the fourth and last case, the patient had been bedridden for many months from acute heart involvement. Two rabbits were inoculated. Both developed acute heart involvement. These sixteen rabbits inoculated with cultures from four patients with heart involvement all developed acute heart involvement.

Other instances which illustrate the nature of the quality that organisms possess, of electing the same tissues that are involved in the patient, are shown in practically all the chapters from 59 to 69 in which are discussed the systemic expressions of dental infections, and in many of which, illustrations are produced of involvements in the animals.

We have in the preceding paragraphs of this chapter discussed the quality of the organism to elect a certain type of tissue. We wish now to discuss the quality of defense and susceptibility of the various organs and tissues of the body in relation to invading organisms. Few of our problems have been so difficult of approach as the study of the nature of these forces which decide what tissues will be selected, and why, in cases of dental and other focal infections. It is only recently recognized, that focal infections may express themselves in other and various tissues of the body. We will approach this subject first by a clinical analysis of the various cases presenting, to determine, if possible, whether there is any inherent force in the individual, or whether it is in the bacterium. Problems 2 and 4, discussed in Chapters 2 and 4, include a study of the nature of invading organisms and susceptibility. In these we found that an analysis of many hundreds of people suggests a classification into three fundamental groups: Those with absent susceptibility, those with acquired susceptibility, and those with an inherited susceptibility, with some tendency to combinations of these types. These also showed that in

HEARTS

R. No.	Material	Date Injected	Date of Death	Case No. and Lesions	Case No.	Percentage with Major Lesions	Heart	Lungs	Liver	Gall Bladder	Stomach	Intestines	Appendix	Kidneys	Urinary Bladder	Generative Organs	Joints	Muscles	Rheumatism Clinical	Nerve Trunks	Spinal Cord	Brain	Eyes	Chloroform
205	C	2–24	6–1	1009	1009	100	x*		x					x					x*					x
220	C	3–8	3–20	Heart			x*											x*	x*				?	
230	W	3–15	3–29	Arthritis			x*																	x
236	C	3–18	4–22				x*		x					x										
237	C	3–18	4–19				x*		x			x		x					x*					
				5 Rabbits			100	0	60	0	0	20	0	60	0	0	0	20	60	0	0	0	20	40
211	C	3–4	3–24	1058	1058	100	x*		x					x			x		x					x
212	C	3–4	3–17	Heart			x*	?	x		x			x			x		x					
238	C	3–18	5–3				x*		x			x		x			x	x						
				3 Rabbits			100	33	100	0	33	33	0	100	0	0	100	33	67	0	0	0	0	33
242	W	3–18	5–24	581	581	100	x*																	x
244	C	3–19	3–29	Heart			x*		x	x		x		x			x*	x*	x*					
251	W	3–23	5–24	Rheumatism			x*											x*	x*					x
269	W	3–31	5–24				x*		x										x*					x
270	C	4–2	4–25				x*	x	x		x	x	x	x				x*	x*					
271	C	4–2	4–7				x*		x	x				x			x*		x*					x
				6 Rabbits			100	17	67	33	17	33	17	50	0	0	33	50	83	0	0	0	0	67
206	C	3–4	6–3	311	311	100	x*												x*					x
223	C	3–9	5–21	Heart			x*	x						x			x*	x*						
				Rheumatism																				
2 Rabbits				Neuritis			100	50	0	0	0	0	0	50	0	0	50	50	50	0	0	0	0	50
Average						100	100	25	57	8	13	22	4	65	0	0	46	39	65	50	0	0	5	48

FIGURE 149.

cases of acquired susceptibility, a large percentage of the lesions were in the nervous system; and in inherited susceptibility, there were both the presence of a lowered defense to streptococcal infection, and a distinct tendency to similar localization in different members of the same family to similar tissue and organ localization.

It is a matter of very great importance whether defense is a purely general quality in which the tissue selected in elective localization is purely accidental selection, or whether that tissue which breaks in a given individual has a predisposition, rather than a predilection on the part of the organism, for that tissue. To determine this, we have analyzed a large number of susceptibility records and case and family records. One of these studies is shown in Figure 150 under the title of "Organ Susceptibility" in which ten patients and their families are used in each group. We have taken ten typical patients each with rheumatism, heart involvements, nerve tissue involvements, and internal organ involvements. In the ten families in which the patients were suffering from rheumatism, we find that the total number of cases of rheumatism in all the ten families is 59. This includes the ten patients, their parents, the brothers and sisters of their parents, the patients' brothers and sisters, and the patients' grandparents, but not the patients' children, since the other parent would furnish half of the influence. The number of cases of heart involvement in all the members of these ten families combined is 7, nerve involvements 19, internal organ involvements 19.

ORGAN SUSCEPTIBILITY

Ten Patients and Families in each Group

	Total No. of These Lesions in Family.				No. of Patients Affected with Lesions			
	Rheumatism	Heart	Nerves	Internal Organs	Rheumatism	Heart	Nerves	Internal Organs
Rheumatism	**59**	7	19	19	**10**	2	4	4
Heart	24	**57**	25	13	6	**10**	7	3
Nerves	15	9	**142**	28	6	2	**10**	7
Internal Organs	13	9	30	**90**	4	0	9	**10**

FIGURE 150.

In the next group, ten patients with heart involvement, the total number of cases of heart involvement in the ten families was 57, of rheumatism 24, nerve tissues 25, internal organs 13. In the ten patients with involvements of the nervous system, the total number of nerve lesions in the ten families was 142, rheumatism 15, heart 9, internal organs 28. In the ten patients with affections of the internal organs, the number of cases of serious involvement of internal organs in all the members of the ten families was 90, rheumatism 13, heart 9, nerves 30.

The second part of this chart shows a similar study limited to the ten patients, not including the various members of their families. In the group of ten with rheumatism there were two cases of break in the heart, four of the nervous system, and four of internal organs. In the group of ten patients with heart involvement six had rheumatism, seven nerve involvements, and three internal organ involvements. In the ten patients with nerve involvements, six had rheumatism, two heart involvements, seven internal organ involvements. In the ten patients with internal organ involvements, four had rheumatism, none had heart involvements, and nine had nerve tissue involvements. It should be noted in passing (and I have discussed it in other chapters), the important relationship between involvements of the nervous system and internal organs.

In Chapter 2, I have discussed the behavior of organisms and have found that they tend very strongly to acquire qualities in accordance with the culture medium; that they do not have physical expression or elective localization in accordance with their biologic classification as members of the streptococcus group. An analysis of the data in Figure 41 of Chapter 4 and also in Figures 42, 43, and 44 of the same chapter, reveals that, with increased susceptibility, there is a marked increase in the number of breaks of the rheumatic group, but that these tend to appear limited to certain tissues in any given individual, but that these tissues differ widely in different susceptible individuals, but in accordance with a common tendency within that family. The constantly heard reference to certain rheumatic lesions, such as that rheumatism and heart involvement prevail in certain families, is borne out in every phase of our study of the more exact relationships in this matter of susceptibility.

In Chapter 4, we recorded that in 681 individuals (being the cases selected from 1400 cases) studied with their families, those cases whose records were considered sufficiently complete to justify comparisons and deductions, all others being rejected, there were 940 cases of heart; and that over half of these appeared in

Susceptibility Group	Average Age	No. of Males	No. of Females	No. of Patients Having Lesions In:							No. of Patients Having Relatives Affected					
				Tonsils	Rheumatism	Heart	Neck	Nerves	Internal Organs	Special Tissues	Brothers	Sisters	Father	Father's Relatives	Mother	Mother's Relatives
Absent	40.7	8	7	4	2		2	2	1	1			4	1	5	3
Acquired	47.9	6	9	6	7	3	8	13	8	8	4	1	2		2	
Inherited 1 side mild	43.4	5	10	8	14	2	9	12	7	7	5	7	9	6	10	9
Inherited 2 sides mild	40.9	3	12	9	13	6	11	12	10	11	9	11	12	7	14	11
Inherited 1 side strong	39.4	4	11	7	14	4	12	15	10	13	5	6	10	6	12	10
Inherited 2 sides strong	33.9	1	14	12	11	12	14	15	14	13	12	11	15	15	15	14

FIGURE 151.

100 families, while over half of the families or groups contained no heart involvement. Figure 151 shows the progressive nature of this quality with the factor of intensity of heredity in a series of groups of individuals beginning with those without susceptibility or those with absent susceptibility, going through acquired susceptibility, to those with strongly inherited susceptibility. From these data, we find strong evidence that the quality of susceptibility, when it obtains as a part of inheritance, tends strongly to be a factor of the organ rather than of the whole system, in which latter case, granting an inherited susceptibility to the rheumatic group lesions, it might be expected to attack organs and tissues entirely at random, in which case the percentage of incidence for given tissues and organs, while they might vary through a wide range in various families, would tend to average similarly in different groups.

In Chapter 21, Influences which Modify Defensive Factors, we found that many forms of overload contributed to causing a break in a particular tissue. We can, accordingly, understand how a nervous system that is overloaded might tend to break; similarly, a heart that is exhausted. It is difficult on such a basis to account for the frequent occurrence of localization in a tissue of the animal corresponding with the tissue that was removed from the patient, but removed because of infection and disease. To illustrate:

A case of an unmarried woman about forty-six with marked

GAN INVOLVEMENT OF GROUPS

Total No of Lesions per Group in:							Total No. of Lesions in Group		Average No. of Lesions per Family		No. of Patients Having:					
Tonsils	Rheumatism	Heart	Neck	Nerves	Internal organs	Special Tissues	Severe	Severe & Mild	Severe	Severe & Mild	Caries	Periodontoclasia	Open	Locked	Rarefying	Condensing
4	7	2	2	7	7	2	16	31	1.07	2.07	6	6	6	9	10	0
6	11	4	9	37	14	15	63	96	4.2	6.4	12	5	5	13	5	3
12	45	13	18	66	28	19	144	201	9.6	13.4	10	5	6	13	5	3
21	61	29	19	92	56	30	227	308	15.3	20.53	14	3	4	12	6	5
16	51	30	27	105	78	31	258	338	17.2	22.53	12	3	3	12	4	5
47	106	77	50	254	106	114	483	754	32.2	50.27	14			13	1	10

FIGURE 151—CONTINUED.

involvement of the cervical and dorsal plexuses (involvement of the neck and upper part of spine) was under study. It was decided that the teeth were involved. They were removed and cultured, and animals were inoculated, with the result that several female rabbits developed acute infective processes of the ovaries, tubes, and uterus. This patient had had first one ovary and tube removed, and later the other ovary, tube, and uterus removed because of acute involvement.

In the chapter on Primary and Secondary Sex Organs, we discuss a number of cases where the tissue affinity involves these organs, and make comparisons with the percentage of incidence of affection of these tissues where the patient was not affected, which latter is almost zero.

This raises the important question as to whether that quality or property of the bacterium, which determines that it shall localize in some particular part of the animal into which it is injected (and which quality has in Chapter 2 been shown to be very transitory and easily lost) is derived from one of the three following factors: First, a condition obtaining in the focus, the tooth in this instance, tending to develop in the organism a quality for selecting this type of tissue; second, the fact that the organ is diseased furnishes to the organisms growing in the focus an appetite or affinity for that diseased tissue, through some substance passing to it through the culture medium, derived from the circu-

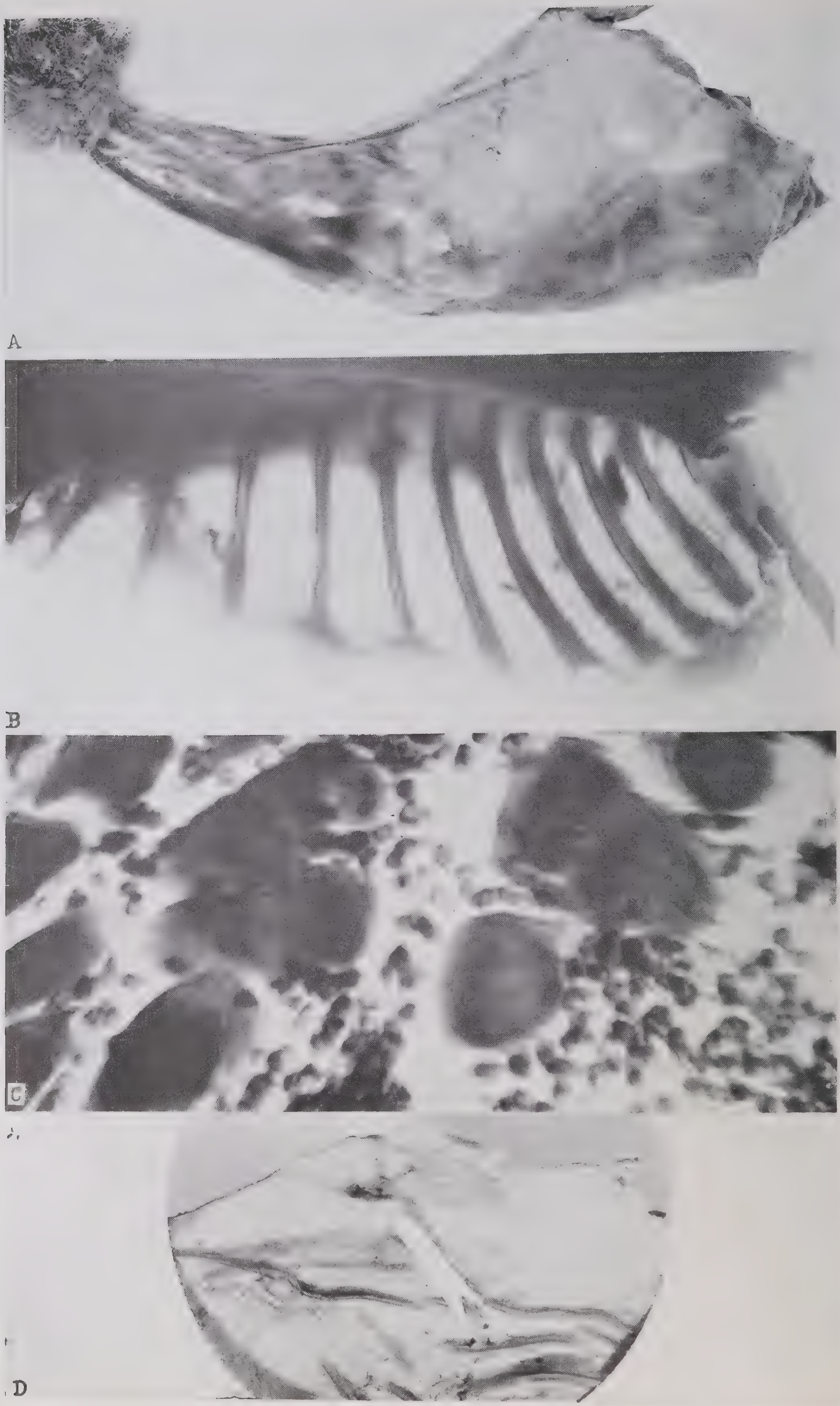

FIGURE 152. SPONTANEOUS HEMORRHAGES CAUSING DEATH IN TWELVE HOURS. A, THIGH; B, CHEST WALL; C, HEART MUSCLE; D, STOMACH LINING.

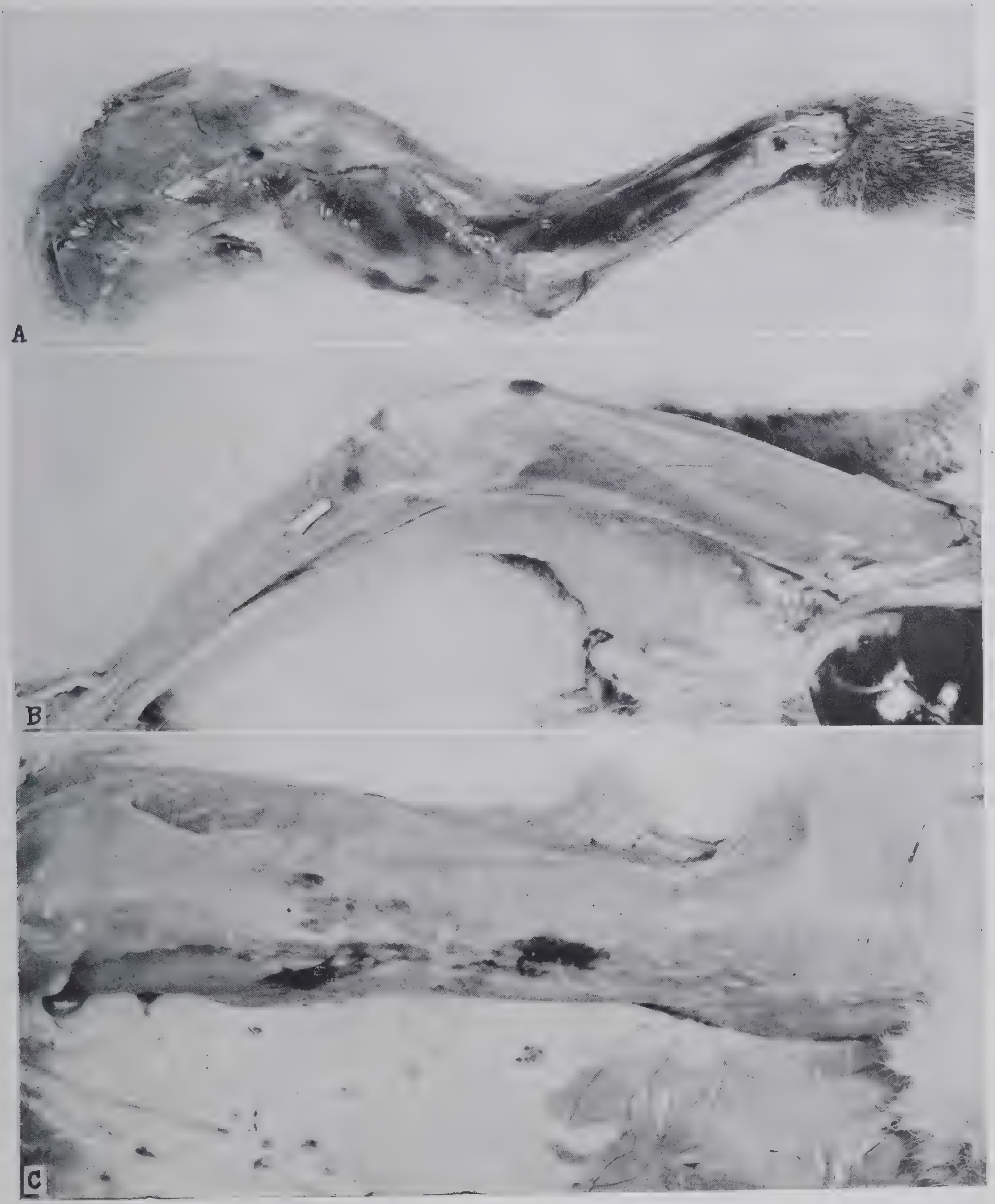

Figure 153. Second rabbit with same culture as Figure 152. A, other thigh of Figure 152; B and C, another rabbit receiving same culture; B, hemorrhage into knee; C, back muscles.

lating blood and lymph; and third, whether normal defense provides in the blood stream a series of defensive factors suited to each and all of the various tissues of the body, the absence of any one of which tends to develop in the blood stream a medium so affecting the organism growing in the focus, that it tends to select that tissue when transferred to a new host. This has suggested a series of studies to determine these factors. In other chapters I discuss the general systemic factors which seem to relate quite similarly to all types of localization. These three problems are so fundamental and the researches that I have made upon them are so extensive that we will discuss them in the three chapters following.

A striking illustration of the decrease in the elective localization quality of a strain is found in the following case history, which is written up in further detail in Chapter 60 (Circulation Disturbances). The patient had been suffering from myocarditis and stomach involvement. Within a few hours after the extraction of his first two teeth, he had a secondary hemorrhage which was very profuse and difficult to control. In fact, he had been kept in the ward after the extraction, both because of the seriousness of his illness and the slowness of the clot formation.

The culture grown from his two extracted teeth, one an infected vital pulp, was inoculated into two rabbits. One of these rabbits (R. 1065) died in twelve hours from spontaneous hemorrhages throughout the body, shown in Figure 152-A, B, C, and D, and also 153-A. A shows the hip and thigh, with multiple hemorrhages; and when the thigh was cut across, or the muscle in any part of the body, these multiple hemorrhages were to be seen everywhere. B shows these multiple hemorrhages in the intercostal muscles; C a section of the heart muscle, with blood cells extravasated between the muscle cells; and D, a hemorrhage into the mucosa of the lining of the stomach. The other rabbit (No. 1064) was chloroformed in twenty-four hours, and showed a similar, but less pronounced, condition. See Figure 153-C. Three other rabbits were inoculated with this culture on the following day. It will be noted that these showed very much less acute and violent reaction than those that were inoculated the previous day, probably due to a difference in the number of generations of organisms that had developed in the new environment, the first generation of organisms always being the most virulent and specific. One of these (R. 1069) was chloroformed in four days and showed subcutaneous hemorrhages in the lumbar region and over the tibiae. This is shown in Figure 154, B and C. Another (R. 1068) showed

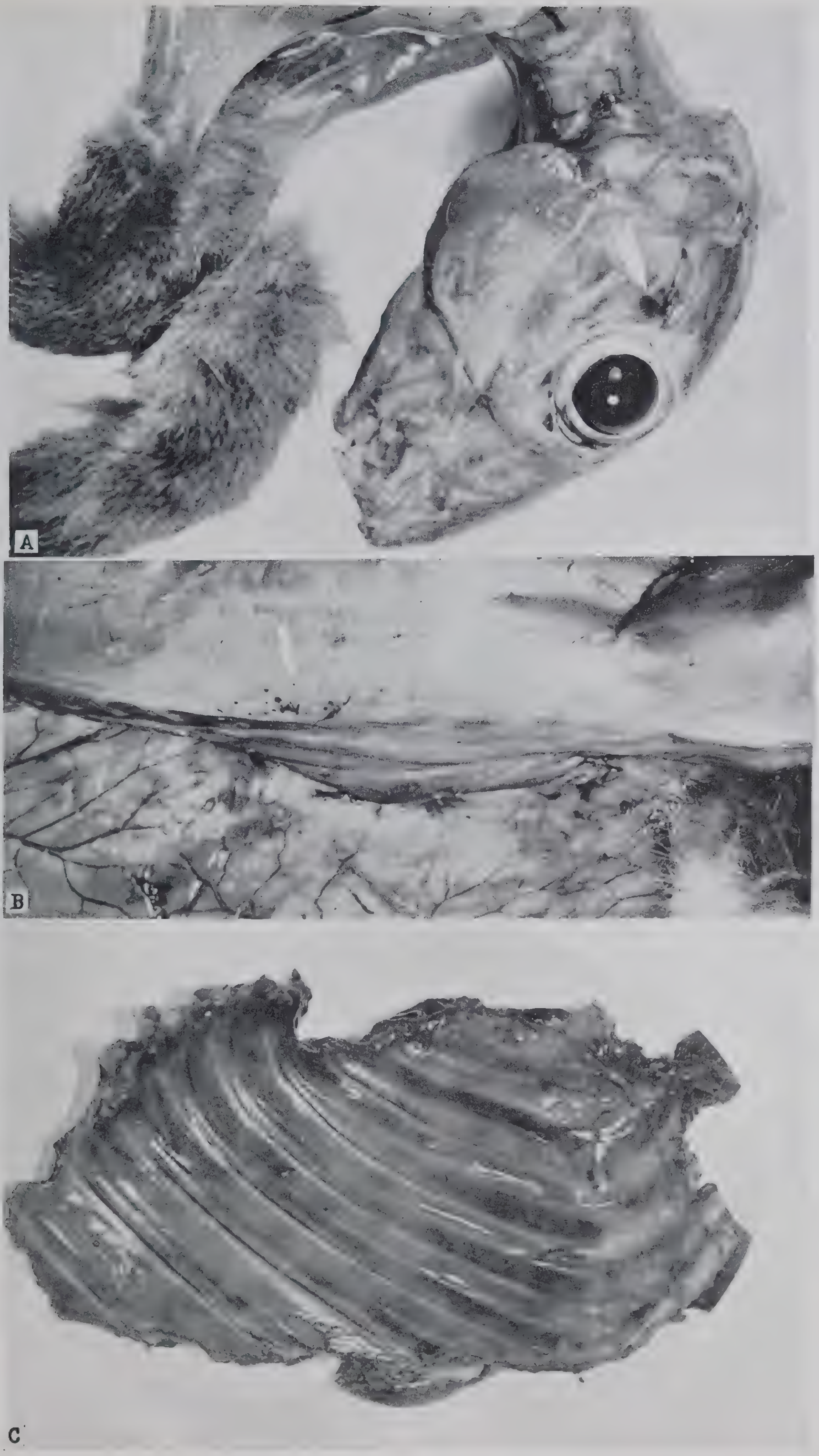

Figure 154. Less severe lesions produced by later generations of same culture. A, hemorrhage from eye; B, back muscles; C, chest wall.

hemorrhages in the muscle tissue of the lumbar region in the back and also the ventral region in the psoas muscle, shown in Figure 153-B. The third (R. 1067) showed a periosteal hemorrhage over the right eye, seen in Figure 154-A. Note that the patient's ailments had been diagnosed as involvements, primarily, of the heart and stomach with expressions in the nervous system.

It is very probable that every culture medium influences to some extent, and in most cases very markedly and rapidly, the elective localization qualities of organisms that are transferred from the host to such artificial media and there multiplied. We would not expect a child, that was transferred from the camp of a savage man-eating tribe to the environment of a modern civilization, would, through its posterity for many generations, exhibit the flesh eating habits of the ancestors. Biologically, the cycle of growth, life, and degeneration, is very comparable in all forms of life, whether it be fourscore years for the man, twenty years for the horse, a dozen for the cow and dog, half that many for the fowl, a day for many moths, and perhaps hours for many of the microörganic forms. However, just as the egg is a resting stage in the life of the fowl, just so the bacterium may take on a condition of suspended animation, or resting stage, in which it may or may not retain its aggressive qualities. In this substance with which we are concerned, the organisms apparently through their wonderful power of adaptation, quite rapidly change in the quality of elective localization and tissue affinity.

SUMMARY AND CONCLUSIONS.

We would summarize the first part of this chapter—namely, The Quality of Tissue Affinity or Elective Localization of Organisms—as follows: The organisms constituting the various strains of the streptococcus group are very different in their main characteristics from microörganisms that produce contagious and infectious diseases. These latter have, in the main, one principal type of expression. The organisms producing parotitis or mumps may also involve some other tissue as the testes, but in the main they tend to select parotid glands; and, similarly, Bacillus typhosus produces typhoid fever with its characteristic involvements of Peyer's patches, enlargement of the spleen and mesenteric glands, and catarrhal inflammation of the intestinal mucous membrane; and, similarly, diphtheria, measles, small-pox, scarlet fever. Unlike these the organisms of this streptococcus group which, in general, find their way into the teeth to establish there a habitat, are often, if not generally, relatively harmless, non-virulent strains. There is probably no one quality which makes this streptococcus so unique and characteristic, as its exceedingly great quality of adaptability to its environment. In Chapter 2 we have discussed this quality of adaptability from another phase and have found that, regardless of the biologic classification, the organism tends to pick out certain tissues of the body in accordance with forces, other than those which establish the biologic differentiations. We also found that they could grow and learn to thrive in the presence of poisons, which originally were so toxic to them as completely to inhibit their growth in one-tenth of the concentration on which they ultimately flourish. Our results of inoculating these strains which have grown for periods of time in infected non-vital parts of the teeth, and sometimes in the vital structures, show these organisms to have taken on qualities of invasiveness which the free strains of the mouth do not obtain and which, doubtless, this organism did not have when it resided in the mouth. We have also found, as shown in Figures 143, 144, etc., that these organisms come to take on a quality, which is, incidentally, very transient and easily lost, of selecting not only a special tissue, when inoculated into rabbits, but very often the same tissue as that from which the patient was experiencing a severe lesion, as heart or kidney, eyes, etc. We also found that this quality of elective localization seems directly related to an acute process; that patients, for example, with acute heart involvements, acute rheumatism, iritis, or retinitis, are more likely to have the organism taken from dental infections, exhibit elective localization qualities, than if the organism is taken from the teeth at a time when they do not have these acute processes.

With regard to the quality of varying defense of a given organ or tissue in different individuals, our studies have seemed to indicate that all organs and tissues tend to have, normally, a high defense for streptococcal involvements; that various types of overload make these special tissues especially susceptible; and also that there seems evidence of the presence or absence of a specific element of defense for individual tissues independent of other tissues of the body, and which defensive quality tends to be similar in different individuals of the same family. In other words, there is strong evidence that the quality of organ and tissue susceptibility follows the laws of mendelian factors. We would, therefore, briefly summarize results of this research as follows:

Dental infections may or may not contain organisms with a specific elective localization quality for certain tissues of the body. When they do so it is generally because the host is suffering, or has previously suffered, from an acute process in that tissue, which acute process frequently, entirely and permanently, disappears with the removal of the focus of infection. There is evidence to indicate that the complete removal of an organ so affected does not destroy that elective localization quality in the microörganism of the focus.

(Note: It should be noted that while I have discussed in the paragraphs of this chapter, the qualities of defense as expressed in organs and tissues, I do not imply, nor do I believe, that defense is limited to these structures. The researches on the nature and quality of the defensive forces in the circulating and other fluids of the body are discussed in other chapters).

CHAPTER XXIII.

THE ENVIRONMENT PROVIDED BY AN INFECTED PULPLESS TOOTH.

PROBLEM: What are the characteristics of the habitat and environment furnished for bacteria in an infected pulpless tooth?

EXPERIMENTAL AND DISCUSSION.

In studying this problem of the particular elements of environment which an infected pulpless tooth furnishes, we will review first some of the characteristics of the tissues involved. The dental pulp and tubuli are filled with cellular and protoplasmic structures such as are included in highly vascularized special tissues. These are contained within bony walls in the form of an almost infinite variety of labyrinths producing such a maze, that if all the tubuli of a single rooted tooth were connected end to end, the total length would constitute three miles of enclosed channels. When we realize the inaccessibility of a large part of this network of intercommunicating channels and canals, we understand why it is so difficult to sterilize a piece of infected dentin even when it is immersed in disinfectants. A streptococcus tends to select necrotic and degenerating tissue elements. Mechanically, a putrescent tooth furnishes a highly ideal hiding place for this germ. It can adapt itself to almost any shape of physical environment in that it may grow so small as to pass through a Berkefeld filter of such fine mesh, that all microscopically visible organisms will be taken out; and these minute organisms which have succeeded in passing through the meshes of this filter, may, on reaching other media, grow to a size that is relatively large for organisms of the cocci group.

Among Nature's most effective mechanisms of defense against this organism, are the phagocyting cells, chiefly the polymorphonuclear leucocytes. These cells have the wonderful property of being attracted to infective organisms, engulfing them, and neutralizing their toxic substance by the antitoxin within their own protoplasms. They may pass through cell walls into the interspaces by the wonderful mechanism of increased permeability of the capillaries in a state of capillary dilatation as a part of the inflammatory process, and after engulfing the toxic substance may retreat from the field of inflammation and pass again into the circulating blood, or be carried away through the lymphatics, chiefly the latter, or in case of an exit, such as an abscess, pass out through the discharge. They are attracted to pathogenic organisms by chemotropism, which is one of the marvels of the entire system of defense. They are completely baffled and helpless when it comes to the matter of entering an infected pulpless tooth to reach and destroy the organism producing the toxic substances, or completely to eradicate the nidus because of the physical environment.

It is difficult to conceive of a parallel where so complete a protection is furnished to an invading enemy parasite entirely within the group of unit cells which, otherwise, would maintain a defense against it; for while the organism is entirely protected from the defensive mechanisms of the body, only one of which are the leucocytes, there is no other source of exit for their poisons and fluids of the host, except as an exit may be possible into the oral cavity through the root of the tooth. In dental practice we undertake to change completely this environment by annihilating the inhabitants of this part of the non-vital tooth structure, assuming that the dentin is non-vital if the pulp is degenerated, and mechanically closing all entrance to this labyrinth and retaining it in a sweet and healthy condition as an inert, if not normally nourished, structure of the human body.

There are several phases of this problem involved in this study, one of which is the nature of the boundary surrounding the dentin of a tooth, particularly the dentino-cemental junction. There has been a great diversity of opinion as to whether or not there was direct communication between the dentin and cementum. (In another chapter I will discuss the matter of direct connection between the dentin and enamel). To determine this we have made a large number of histological sections, before speaking of which, however, we wish to refer to the excellent work of others, particularly that of Dr. Harold Box,[13] of Toronto. He seems to have demonstrated to his complete satisfaction the presence of communicating channels between the dentinal tubuli of the dentin and the canaliculi and the lacunae of the cementum. Marshall, on the other hand has furnished

[13] See bibliography.

evidence which has seemed to demonstrate to him that the cementum is laid down upon the dentin as an entirely independent structure, completely separated from it. Mummery, Hopewell-Smith, Williams, Boedecker, and many others, have discussed the relationship of the dentin to the surrounding structures with especial consideration of the problem of nourishment of tooth structure. Our own studies indicate that, in general, the cemental border of the dentin and the dentinal border of the cementum constitute what is apparently the same tissue, though in fact like a common fire-wall built by two different contractors, with occasional openings for communicating channels extending from one side to the other, which openings, however, constitute a relatively small part of the total area in this common wall, and which openings seem generally, if not nearly universally, to be special channels extending from the pulpal tissue to the peridental membrane, and which may have little, if any, communication by anastomosis, with either the dentinal tubuli of the dentin or with the lacunae and canaliculi of the cementum. They are, in effect, either very minute or larger multiple foramina.

As one of several studies on this phase of the problem, I have placed metal tubes in the pulp chamber from the apex of the tooth, carefully cementing same, and have passed various fluids into the tooth under measured pressures. Several substances were tested, and it was found that both the sodium and the chlorine ions would pass from the pulp chamber of a freshly extracted tooth through both the dentin and cementum, and the dentin and enamel, in easily measurable quantities. Among the easily passed ions was that of the calcium.

When we study various tissues of the body, we find their function is determined by certain inherent qualities pertaining characteristically to their cells. For example, whereas the various soluble products that are found in urine are entirely inhibited from passing through the tissue constituting the bladder wall, that same fluid will pass with great freedom and rapidity through the wall of the small intestine; and similarly, the various glands and organs of the body have cells adapted to hold back certain substances and allow certain others to pass. In general, this problem is referred to as semipermeability, and it has to do with the function of every individual cell, as well as every type of cell, and is different in different tissues and cells. Electrolytes can pass through most membranes of the body; colloids through but few of them. Hence the colloids of the blood stream cannot pass through the blood vessel walls, not even through the capillary walls, though the electrolytes can. When the colloids, which are largely proteins, are split into the various amino acids, they may pass through tissue cells in accordance with the structure of that molecule and the function of the cell in question. Each cell, therefore, may be thought of as a lock which takes a certain type of key. The various molecules of various compounds can be thought of as the key, and only those fitting the particular combination in question, pass to that particular tissue. But electrolytes and certain of the amino acid groups and their derivatives, will pass through tissues which are impervious to colloids and to bacteria.

My studies of the dentino-cemental junction have led me to believe that certain substances can pass readily through this boundary, while the bacteria cannot. By placing organisms grown from infected teeth in sealed glass tubes, they very soon cease to multiply, and in a very short time nearly all are dead. Only a minute orifice is necessary to change quite completely the per cent of dead organisms. I have had sections cut from normal tooth structures, and have used these as semipermeable membranes to determine, if possible, whether or not food materials may pass through this structure while organisms may not, by connecting through glass tubes an infected and sterile culture medium, separated only by this partition of tooth structure, including the continuous wall of dentin and cementum cut from a suitable tooth. While these studies are not completed, the evidence available indicates that nutrient material can pass to the organisms through this structure, but that the organisms themselves cannot pass. If this be true, the tooth in all probability furnishes a protection for the organism, in that neither the leucocytes nor the defensive bactericidal elements of the blood can reach the organisms within the dentin. The organisms in that position may receive a continuous supply of nutriment through the semipermeable, but to them impenetrable wall, making the boundary to the dentin. They are here completely protected to produce a toxic substance which may pass to the host and continually irritate and injure the defensive forces of the host. If those defensive forces be sufficiently adequate to neutralize all toxic products immediately within the vicinity of the tooth, the warfare will be limited to that zone. This battle-ground and the battle are discussed in other chapters. If the products are not neutralized in the immediate vicinity of the tooth, because of the host's temporary or permanent inability to make that type of warfare, they may pass to the various organs and tissues of the body and irritate or sensitize them. The tooth, then, must be looked upon as an entirely different structure from flesh or living bone, since, if the pulp is dead, Nature has no mechanisms for disinfecting the dentin after it becomes infected, or of maintaining it if it is non-vital but sterile. She is compelled to make the warfare in the form of a quarantine about the tooth until such time as she can either absorb it or exfoliate it. A pulpless tooth is, therefore, a sequestrum; and if it becomes an infected sequestrum, must be dealt with as a foreign substance and not as a part of the host.

An important question has been the matter of transfer of fluid from the dentin to the cementum or the enamel, or through both of these from the pulp to the fluids surrounding the different structures of the tooth. Bunting and Rickert[14] have demonstrated the passage of fluids from the inside to the outside of a tooth.

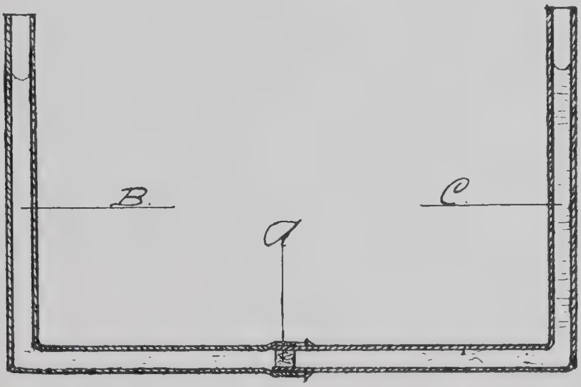

FIGURE 155. DIAGRAM OF THE APPARATUS WHICH USES A SECTION OF TOOTH AS A PERMEABLE MEMBRANE. A, TOOTH SECTION; B AND C, CONTAINERS FOR SOLUTIONS BEING TESTED.

Figure 155 shows the set-up of one of the experiments for determining the permeability of tooth substance for nutrient products in culture medium on one side of a sac of the tooth structure, and living organisms in a normal salt solution on the other. The organisms will not increase in number in normal salt solution to any very great extent. In the arm of the apparatus to the left, we have placed the sterile culture medium. If the organisms may pass through a sac of dentin and cementum, containing at least one, and in some instances two, dentino-cemental borders, they can go from the salt solution to the culture medium. By culturing from time to time, as well as by its appearance, we can determine the development of organisms on the medium side. If there chances to be a multiple foramen, and some teeth have as high as seventy-five, they may pass through these and not have to pass the true dentino-cemental boundary. If the infected normal salt solution remains clear and if its total bacterial count per cubic millimeter does not increase, we can assume that organisms have not developed more rapidly than they have died off. If, on the other hand, the culture medium is able to pass to the salt solution, either in whole or only some of its contained products, the organisms may multiply. We have run several kinds of controls. All of these set-ups were autoclaved. Some have normal salt on both sides, one infected and the other not; some distilled water on one side and the other concentrated salt solution, to determine whether the tooth under these circumstances would act as a semipermeable membrane. Some contain electrolytes on one side and culture media on the other; others colloids.

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[14] See bibliography.

SUMMARY AND CONCLUSIONS.

From the data here available it is suggested that the dentino-cemental border, under ordinary conditions, is an impenetrable barrier to bacteria; that while the organisms cannot pass through it, toxic substances produced by the bacteria can, the extent of which is not yet completely determined; that while the organisms cannot pass through this dentino-cemental boundary, nutrient substances from culture media surrounding the tooth can pass through this boundary. This boundary also forms a quite complete barrier against the defensive forces of the body, such as phagocyting leucocytes, bactericidins, etc. The tooth, therefore, furnishes an environment which is particularly favorable to the invading organism and unfavorable to the host, in that the former is protected from the aggressive defensive forces of the latter, while able, by the natural laws governing the behavior of liquids and gases, to secure a continuous supply of nutriment through the walls of the fort. The placing of an infected tooth beneath the skin of the rabbit is many times more dangerous to the rabbit than the introduction of that bulk of concentrated infected culture; and even though an infected tooth with apparently splendid root filling is thoroughly sterilized externally and placed beneath the skin of a rabbit, within a few days it shows evidence, by changes in the hematology and chemistry of the blood, of a progressive destructive change, which, in the majority of instances, terminates in death within two weeks. We would, therefore, change our conception of the significance of an infected tooth about as follows: from

> "(*Old interpretation*) *Since the presence or absence and the extent of danger of infection in a suspected tooth, are determined by the size of the pus sac at the end of the root, those teeth are dangerous which have this mass of infection external to the end of the root, and in proportion to its extent; and those are not dangerous which have little or no pus sac.*" to
>
> **Since an infected tooth is a fortress for bacteria within the tissues of the host, and since, in accordance with the laws governing the behavior of solvents and solutes, the dissolved substances within the tooth can pass to the outside of it, and, similarly, the dissolved substances outside the tooth can pass to the inside of it, together with the fact that the defensive mechanisms of the body are quite unable to enter and reach the bacteria within the tooth except in exceedingly small numbers through the natural openings of the root, which openings will, however, permit the organisms to pass at will from within the tooth to the outside, we must conclude that an infected tooth furnishes a condition and environment that is tremendously in favor of the invading organism inhabitating it, as compared with the host, since the latter may only rid itself of the menace by exfoliating it or absorbing it.**

CHAPTER XXIV.

ELECTIVE LOCALIZATION AND ORGAN DEFENSE. PART ONE: INFLUENCE OF DISEASED TISSUE ON ORGANISMS IN THE DISTANT FOCUS.

PROBLEM: Do diseased organs and tissues modify bacteria growing in the distant focus, or create in them a capacity for elective localization for those diseased tissues?

EXPERIMENTAL AND DISCUSSION.

This is an exceedingly difficult but very important problem, for if it is true it not only removes from the organisms some of the culpability but furnishes an explanation for some of the phenomena which develop by transferring the organisms from that focus to another host. An analysis of our clinical records and experimental data throws some direct light upon this problem. In the second chapter preceding I reviewed a case in which the bacteria from the dental infection of a patient suffering from acute involvements in the cervical and dorsal regions, when inoculated into experimental animals, developed acute involvements in the ovaries, tubes, and uterus, a lesion that is so rare, that not one per cent of experimental animals develops such a lesion from dental cultures of ordinary patients. Indeed, it had not been revealed in the taking of the physical history that this woman had had these operations, a secret which she carefully guarded. After the development of the lesions in rabbits, I asked her specifically regarding the history of disturbance in pelvic organs, when she gave me the history that one ovary and tube had been removed some years previously at one operation, and at a later time the other ovary, tube, and uterus. In this case, then, there were no such tissues to be involved.

In Chapter 62 on "Primary and Secondary Sex Organs" we report a case with a very similar history. The woman presented with a heart involvement and rheumatism quite severe. The inoculation of the rabbits developed acute involvements in the ovaries, tubes, and uterus, with an unusually severe involvement of the uterus with extensive suppuration. I sent for the patient and asked her if she had given me the history correctly. She said she had not and that she did not wish to think about it, let alone talk about it, since a purulent uterine discharge had been becoming more severe for six months and her physician had advised her that it was probably malignant and at her age an operation would not be justified. In this case, as shown in that chapter, this purulent discharge completely subsided with the removal of her infected teeth and has not recurred in two years except for a couple of days at the time that an infected sequestrum was giving trouble after one of the extractions. Had the infected uterus been the primary lesion we would not expect that the removal of the dental infection would have seriously modified the primary focus, which is very important.

In that same chapter we recite a case of a man from whose dental infection the cultures were taken and inoculated into rabbits, and which produced acute infections in the testes of each of three male rabbits, the culture being taken from three different teeth. On being questioned, his reply was "Can't a person have any secrets?" and confessed that he had had a recent severe involvement of the testes; that he had had gonorrhea twenty years previously which had been treated and supposedly cured.

In that chapter we refer to cases of ovarian cyst that have been operated and in which cases the cultures from dental infections developed ovarian cysts in the rabbits.

It is not possible to state from these clinical cases to what extent either the dental infection was originally causative in the involvement of these special tissues or to what extent these special tissues influenced the organisms growing in the focus. In the first case mentioned, however, it was seven years since the last operation; in other words, this individual did not have in her body primary sex organs to be related directly to the dental infection. It is true, however, that the dental infections which were removed had been of probably twenty years standing and her first operation had occurred fifteen years previously.

These data suggested some special studies which were conducted as follows: Tissues were taken from several different organs of the rabbit's body, macerated and placed in culture media inoculated with the same organism, a passive strain which, when it grew out, was inoculated into a series of rabbits, and careful macroscopic and microscopic studies were made to ascertain if the placing of healthy tissue of a given organ would tend to create in the bacteria an appetite for that tissue. These results were all negative, which we interpreted as meaning that a normal healthy organ did not contribute elective localization qualities to organisms growing in a focus; and that if such condition does obtain—namely, that the infected organ develops the elective localization quality in a distant focus through the influence of that organ on the culture medium—light might be gotten on this phase of the subject by the placing in the culture medium of some of the diseased organ tissue from an animal developing a severe lesion, as a result of inoculation of the animal. Since the organism which produces such a lesion does in many instances do so in several animals, it is evident that the organism had to that extent the power of elective localization. When, then, a diseased organ tissue is used for modifying a culture medium to determine whether or not that tissue will influence the organisms growing in that medium, that diseased tissue carries with it some of the original organisms having that quality. It is, therefore, important to note that, when cultures are taken from diseased organs, which have become so because of elective localization qualities of bacteria, those cultures tend to produce lesions in that same tissue in the next animal passage, which quality we have assumed they were maintaining and not acquiring, having brought it from the original focus. We are, then, practically in the same position when we take a piece of diseased and infected organ to modify media, that we would be if we took the organisms without the tissue, in which we would expect elective localization qualities. This, therefore, makes it impossible to determine with this experiment whether an infected diseased organ, which disease was not produced by the dental focus, would so modify the organisms in a dental focus as to establish elective localization qualities.

We have made many inoculations with organisms grown from the lesions which have developed in rabbits from dental infections, and have seen many instances suggesting strongly that the organisms still had elective localization qualities. A first requisite for this experiment is to develop an acute or chronic lesion by any process in an internal organ; and, after it is well established, to establish a dental condition which would tend to become infected from the blood stream. To accomplish this I have undertaken the following experiment:

Since we frequently find teeth, as illustrated in Chapter 63 on "Kidneys and Related Excretory Organs" which, when removed from the mouth of a patient having acute nephritis and placed under the skins of rabbits, produce acute kidney involvement which can be definitely identified by the presence of albumin and casts, and later verified by macroscopic and microscopic study, as shown in that chapter, we must consider the matter an open question until further data are available, the experiments for which are in progress.

I wish to insert a warning at this point: Judging from the observation as to the conclusions that are liable to be made by persons who undertake to check an experiment of this kind, I shall anticipate that some persons will undertake to put teeth under the skins of rabbits to determine whether or not it is possible by this process to accomplish this result. They may have negative results which, I shall anticipate, they will conclude are a proof that there was an error in my experiments. My warning is twofold: Firstly, that just as all individuals that have infected teeth, do not develop kidney involvement, just so all rabbits that have inoculations made by any form do not always develop lesions; and, secondly, all cases of nephritis are not caused by dental infection, and the tooth may be selected either from such a patient, or it may be a tooth with an acute apical involvement, and the kidney lesion a chronic one, in which case it will usually be true that the dental infection will not show marked elective localization qualities.

There is another source of information, however, which is very important in answering this problem. The studies reported in the various preceding chapters, particularly Chapter 4, had to do with the particular tissue that tends to break in individuals with an inherited susceptibility, in which case they tend to break in the same tissues as did their ancestors and as do their brothers and sisters. It is abundantly demonstrated that this quality is transferred from generation to generation entirely regardless of its acute development in any particular link in the chain, in which case, if the individual was a carrier only of the quality without having had that lesion develop or a lesion in that organ develop, it could not be said that a diseased organ had had anything to do with the quality of elective localization, since that was neither evidence of organ involvement nor of focal infection. It becomes clear, then, that this quality is something inherent within the individual, which is transferred from generation to generation, which may skip, in accordance with the mendelian laws, individuals who themselves may be carriers of the quality.

PART II. NATURE OF THE DEFENSIVE MECHANISMS.

This brings us to the second phase of this problem: namely, whether normal defense provides in the blood stream a series of defensive factors suited to each and all of the various tissues of the body, the absence of any one of which tends to develop in the blood stream a medium so affecting the organism growing in the focus, that it tends to select that tissue when transferred to a new host.

This is a very difficult but very important problem, since a knowledge of these factors is essential for an explanation of the phenomena that develop in clinical practice in the study of the various types of reaction, and of complete absence to reaction from dental infections. In this statement of the problem we have a distinctly different situation from that in the preceding paragraphs of this chapter in which we discuss the ability of a diseased organ to produce in the bacterium an appetite and quality of localization for that diseased organ, when the organism is transferred to a healthy host. In this part of the chapter we are not dealing with the presence of a definite substance which is the product of a diseased organ, but with the absence of some substance which, if present, would constitute defense, but whose absence constitutes susceptibility.

A line of approach to this question is suggested by the experience of the eskimos in northern latitudes. It is said, for example, that in some of the North Sea Islands every eskimo, who became exposed to measles, died. We cannot say, however, that this was so because there was generated in his body some specific substance which made him susceptible, for history shows, that for centuries on these same islands, no eskimo died of measles because none were exposed to it. It is apparent that his absence of a defense, which the white races have in part built up through a process of infection in each generation and therefore of a transmitted immunity, is entirely due to a lack in his constitution of some qualities which, if present, would constitute defense, but which defense he did not require in the absence of being exposed to the contagion; in other words, the absence of a positive factor rather than the presence of a positive factor.

When we study, then, our carefully worked out clinical histories in their relation to presence and absence of defense, as we have done in Chapter 4, and their relation to the particular types of

CHARACTERISTICS OF ACTIVE AND DEFICIENT IMMUNITY

Susceptibility Group	*Characteristics of Dental Lesions*	*Susceptibility to Systemic Involvements from Dental Infections*	*Caries*	*Periodontoclasia*	*Blood Calcium*
Absent Susceptibility	Marked rarefying osteitis	None	Slight	Marked tendency to	Ionic calcium high
Acquired Susceptibility	Rarefying osteitis surrounded by condensing osteitis	Generally absent but recent acute attack	Recent acute	Previously a tendency; is latterly not extending	Generally high, recently lowered
Mildly Inherited Susceptibility	Mild or slight rarefying osteitis	Recurring attacks	Recurring through life	Very slight	Generally lowered
Strongly Inherited Susceptibility	Slight rarefying osteitis with marked tendency to condensing osteitis	Frequent and severe attacks	Chronically severe	Practically almost absent	Chronically low

FIGURE 156.

expression which the same infection tends to produce locally about the infected teeth in these different groups, and compare these with the blood chemical analyses, saliva analyses, etc., of the individuals of these groups, we find that we are dealing in the main with individuals having very definitely differentiating qualities, already reviewed in Chapter 4. We find evidence that this quality of complete defense, or, at least ample to defend the individual against systemic involvement for the major part of a lifetime from even several dental infections, has many identifying characteristics. If we group these various differentiating qualities for the different groups of individuals according to our classification, we find a condition as shown in Figure 156. There are many other important factors which are variable in these various groups, one of which, and perhaps the most important of all, variations in the defensive mechanisms of the blood in these various groups, is discussed in Chapter 41.

SUMMARY AND CONCLUSIONS.

We are led to conclude from the available data, that we do not as yet have sufficient information to draw a close distinction between the influences of the organisms on the affected organ, in contradistinction to the influences of the diseased organ upon the organisms in the focus. The available data suggest strongly, if they do not definitely indicate, that both these conditions exist, in some instances, either one acting entirely alone, and in some others there are indications that both exist at the same time. These data have suggested very definite researches that are being organized to throw further light upon this subject.

CHAPTER XXV.

THE RELATION OF THE TYPE OF REACTION TO THE NATURE OF THE IRRITANT, BACTERIAL OR TOXIC.

PROBLEM: Have we different products from dental infection?

EXPERIMENTAL AND DISCUSSION.

In Chapter 17, we have discussed the presence of non-bacterial poisons of dental origin; and in Chapter 24, we have discussed the quality of bacterial invasion and its elective localization. This research was undertaken to determine what, if any, relationship there is between the type of systemic disturbance and the nature of the irritant. One method of procedure has been to take from the teeth of patients suffering definite and acute systemic involvements, both the organisms growing therein, and the soluble poisons present in those teeth, and injecting these into experimental animals. In Chapter 18 under the discussion of "Studies of Pulpless Teeth," I presented a chart showing the effects on animals of injections with the washings from crushed infected teeth, both with and without filtering, and have compared these with the effects on animals of cultures grown from teeth (Figure 24, Chapter 2), either the same or similar ones, both when in media in which they were grown, and when removed from media and washed with several changes of normal salt solution and then inoculated in a normal salt solution suspension. By referring to those charts, it will be seen that the average length of life of animals injected with the washings of the teeth, was less in this group than in the groups inoculated with the washings plus the organisms, and also less than when injected with the culture of the organisms without the toxic substance from the tooth, whether the organisms were washed or injected in the medium in which they have grown. These figures were as follows:

The average length of life of 13 animals inoculated with filtered washings from teeth, was 5 days; as compared with the group with unfiltered washings in which 8 animals died with an average life of 12 days. In the third group of 8 animals, inoculated with the organisms washed and suspended in sodium chloride, the average length of life was 7 days; and in fourth group of 71 animals, in two series, 16 in the first and 55 in the second, receiving whole culture, (these organisms in the medium in which they grew, approximately 1 cc. doses), in the first series of 16, the average length of life was 6 days, and in the second group of 55 was 7 days. In another chapter I have suggested an explanation for the phenomenon of the toxic substance killing in less time than the toxic substance plus the organisms producing it.

In our various efforts to study in a comparative way the injurious effects of toxins and bacterial invasions, the comparisons have been more largely between miscellaneously selected toxins and miscellaneously selected dental cultures. I have, accordingly, undertaken to check this more closely by extracting the toxin from given teeth for inoculation as washings from the tooth in one group of animals, in some cases filtered, others not filtered, and comparing these effects with homologous cultures by growing the organisms from the particular tooth from which the toxic substance had been washed. A group of these is shown in Figure 157. In the group showing changes in weight of rabbits inoculated with tooth washings, seven—namely, the sixth, seventh, eighth, tenth, eleventh, twelvth, and thirteenth,—were filtered washings, and the others of that group—namely, the first, second, third, fourth, fifth, and ninth, — from unfiltered. In this group the average loss in weight per rabbit was 131 grams and the average percentage loss 11½. In the group inoculated with the culture from these same teeth, the average loss of weight per rabbit was 180 grams and the average percentage loss 17. It will be noted that in this series the loss in weight was more rapid where they received the whole culture, that is 1 cc. of organisms and culture medium from a twenty-four hour growth, than where they received washings from the single tooth only. The difference, however, was one of degree, for the effects were very serious with both. This suggests that when a patient is receiving the toxic material into the system in addition to the bacterial invasion, the injury would be distinctly worse than to receive either one alone. It is of interest to note that in this group of nine rabbits inoculated with washings, the rabbit that lost the greatest amount, both in total grams and in percentage—namely, number eight—received a filtered washing. This corresponds with some of the data shown in other studies which demonstrates that the toxic material in some teeth is extremely injurious, for the length of time required

COMPARISON OF TOOTH TOXIN AND TOOTH CULTURE

A. Tooth Washings

Case No.	Rabbit No.	Tooth Washing Unheated		No. of Days Lived	Weight Changes					
					Gain		Loss		% Gain per day	% Loss per day
		Filtered	Unfiltered		Actual	%	Actual	%		
433	145		"	11			44	3.9		0.4
891	274		"	10			194	18.0		1.8
1014	285		"	6			170	19.4		3.2
1014	294		"	9			0	0.0		0.0
1081	288		"	11			90	9.4		0.9
1149	592	"		1			15	1.3		1.3
1149	593	"		14*			14	1.0		0.1
1157	542	"		4			278	24.0		6.0
1153	545		"	34*	124	10.4			0.3	
1171	607	"		11			510	34.5		3.1
1123	621	"		6			191	25.0		4.2
1177	640	"		7			263	21.0		3.0
1412	753	"		49*			59	4.9		0.1

B. Tooth Cultures

Case No.	Rabbit No.	Culture		No. of Days Lived	Weight Changes					
					Gain		Loss		% Gain per day	% Loss per day
		Whole	NaCl Suspension		Actual	%	Actual	%		
433	146	"		10			309	27.1		2.7
891	275	"		32*			334	25.9		0.8
1014	289	"		5			166	18.6		3.7
1014	293		"	22			227	30.6		1.4
1014	294		"	9			163	20.5		2.3
1081	291		"	43	10	1.3			0.1	
1149	594		"	11*			148	13.6		1.2
1149	595		"	13*			13	1.0		0.1
1149	596		"	10			535	39.6		3.9
1149	597		"	11*			105	11.1		1.0
1157	544		"	12			144	16.5		1.4
1153	549		"	9			230	24.5		2.7
1153	550		"	7			318	27.5		3.9
1171	606		"	14			174	18.5		1.3
1123	613		"	21*			73	6.0		0.3
1177	643		"	17*	154	14.5			0.9	
1412	755		"	9			329	31.0		3.4
	756		"	3			137	13.5		4.5

* Chloroformed

FIGURE 157.

for this rabbit to lose 24 per cent in weight was only four days. The average percentage loss per rabbit per day for the group receiving the washings was 1.8 and for the group receiving the inoculations of the cultures of the same teeth was 1.9 Another rabbit of this series, No. 592, receiving the filtered washings of a tooth, died in one day. On this account, it will be seen it is not sufficient to judge total loss, since a rabbit may be killed so quickly by the toxic substance of a filtered washing that it does not have time to lose in weight.

SUMMARY AND CONCLUSIONS.

The evidence available indicates that infected teeth elaborate two distinctly different products, one being bacteria, and the other a toxic substance or group of toxic substances, which, independently of the organisms developing them, may produce various and profound disturbances in tissues in various parts of the body, one of the important group of disturbances being that of the blood stream.

CHAPTER XXVI.

CHEMOTAXIS AS A MEANS FOR INCREASING DEFENSE.

PROBLEM: Can defense for streptococcal infections be increased by introducing enterally or parenterally (by ingesting or injecting) chemicals?

EXPERIMENTAL AND DISCUSSION

For hundreds of years the natives of Peru have been fighting malaria by chewing the bark of various species of cinchona trees containing the active principle of quinine. Modern science has perfected the process, and now injects into the circulation of the affected person, derivatives of that original compound, which are conceived of as having specific action on the plasmodium which produces malaria. This might be looked upon as true chemotaxis. Similarly, Ehrlick developed the administration of compounds of arsenic, known as "606" or salvarsan, which, under certain conditions, tends to be specific for treponema pallidum. Still later, compounds have been made of chaulmugra oil, which have very specific action in the treatment of leprosy. Similarly, Wright and others have used ethylhydrocupreinhydrochlorate in the treatment of pneumonia, particularly in epidemic form, which is disastrous in the mining districts of South Africa.

With a view to determining whether or not some such products enhance the defense of rabbits inoculated with cultures of dental origin, we have made several studies in order to determine more exactly the effect of the medication. We have studied the morphology of the blood before and after its use. The chart in Figure No. 158 shows the result of a series of inoculations made with ethylhydrocupreinhydrochlorate. The procedure of the experiment was as follows:

The rabbits of a group of eight were inoculated with decreasing doses of a culture which was grown from a tooth of a patient suffering from an acute eye involvement. This culture was selected because of its uniformly fatal termination with dilutions from one cubic centimeter to one-eighth of a cubic centimeter of culture. The rabbits of this group are shown in Section I of the

CHEMICAL MEANS FOR INCREASING DEFENSE.

Case No. 1131

R. No.	Chemical		Amount of Culture cc.	Method of Inoculation	Days Lived	Death	
	Amount cc.	Dilution				Spontaneous	Chloroform

Section I. Eight Control Rabbits.

458			1.0	Intra-V	½	*	
461			1.0	Intra-V	1	*	
444			1.0	Intra-V	1	*	
447			1.0	Intra-V	1	*	
457			1.0	Intra-V	1	*	
465			0.5	Intra-V	1	*	
468			0.25	Intra-V	½	*	
469			0.125	Intra-V	3	*	

Section II. Rabbits Injected with Ethylhydrocupreinhydrochlorate before Culture.

407	1/10	1%	1.0	Sub-C Intra-V	10	*	
427	1/10	1:5000		Sub-C	10		*
*428	1/10 1/10 1/10 1/10	1:1000 1:100 1:1000 1:5000	1.0	Sub-C Sub-C Sub-C Sub-C Intra-P	98		*
481	1	1:100	0.25	Intra-V Intra-V	30	*	
484	2	1%	0.5	Intra-V Intra-V	67		*
485	1	1%	0.5	Intra-P Intra-V	14	*	
486	2.5	1%	0.5	Intra-V Intra-V	78		*

Section III. Rabbits Injected with Ethylhydrocupreinhydrochlorate after Culture.

482	1.0	1%	1.0	Intra-V Intra-V	1	*	
487	3.0	1%	0.5	Intra-V Intra-V	1	*	
512	1.5	1%	0.5	Intra-V Intra-V	1	*	

Section IV. Rabbits Injected with Culture and Ethylhydrocupreinhydrochlorate Simultaneously.

490	3.0	1%	0.5	Intra-V	23	*	
510	2.5 1.0 1.0	1% 1% 1%	1.0	Intra-V Intra-V Intra-V	15+		

* Rabbit 428 received both chemicals.

FIGURE 158.

CHEMICAL MEANS FOR INCREASING DEFENSE

Case No. 1131

R. No.	Chemical		Amount of Culture cc.	Method of Inoculation	Days Lived	Death	
	Amount cc.	Dilution				Spontaneous	Chloroform
Section V. Rabbits Injected with Ethylhydrocupreinhydrochlorate Alone.							
521	1.0	1%		Intra-V	29		*
522	1.0	1%		Intra-V			
	1.0	1%		Intra-V			
	1.5	1%		Intra-V	54		*
Section VI. Rabbits Injected with Chaulmugra Oil Compound before Culture.							
488	2.0		0.5	Intra-P	70		*
492	1.0			Intra-P			
			0.5	Intra-V	45	*	
*428	1.0		1.0	Intra-P	79		*
Section VII. Rabbits Injected with Chaulmugra Oil Compound Alone.							
477	2 m.			Sub-C	28	*	
480	1 m.			Sub-C			
	1 m.			Sub-C	54		*
250	1 cc.			Intra-P			
	2 cc.			Intra-P	36		*

* Rabbit 428 received both chemicals.

FIGURE 158 CONTINUED.

chart, in which it will be seen that all of the rabbits died in from twelve hours to three days, all but one in one day or less. The rabbits which did not die during the work hours of the day on which they were inoculated, but were dead on the following day, were recorded as having lived one day. It is probable that several of them that are recorded as having lived one day, really lived much less than a day. The average, therefore, for the group would probably be pretty close to one day, which was too short a time for changes to take place that could be recorded as percentage loss in weight per day.

Section II shows a group of seven rabbits that were inoculated with the indicated quantities of ethylhydrocupreinhydrochlorate prior to their receiving the indicated quantities of the same culture as the rabbits in Section I, and it will be seen that most of these rabbits were still living in from one to two months, when they were chloroformed for tissue sectioning and study; and, whereas, one-eighth of a cubic centimeter of this culture sufficed to kill without the assisting protection of ethylhydrocupreinhydrochlorate, those receiving it were enabled to withstand eight times that lethal dose for weeks or months.

In Section III we have a group of three rabbits that were injected with ethylhydrocupreinhydrochlorate after, instead of before, receiving the injection with the culture, and it will be seen that these rabbits all died spontaneously within a day. In other words, the administration of this chemical after the inoculation had had an opportunity to establish itself, failed to reinforce the defenses of the body sufficiently to stamp it out or to protect the animal from its ravages.

In Section IV we have two rabbits that were inoculated with the culture and ethylhydrocupreinhydrochlorate simultaneously, the first one of which lived twenty-three days, and the other was still in good condition in two weeks.

In Section V we have two rabbits that received ethylhydrocupreinhydrochlorate alone, and one of these was chloroformed in twenty-nine days and the other in fifty-four days, to ascertain the effect, if any, of the chemicals.

Section VI shows three rabbits that were injected with chaulmugra compounds before the culture, and it will be seen that the first one was chloroformed in seventy days, another died in forty-five days, another was chloroformed in seventy-nine days.

Section VII shows three rabbits that received the chaulmugra compounds alone without the culture. The first rabbit died spontaneously in twenty-eight days, the second was chloroformed in fifty-four days, and the third was chloroformed in thirty-six days.

From these data it will be apparent that these chemicals have shown evidence of reinforcing the defense of the rabbits against this culture which was taken from the infected tooth. The tooth itself was not giving the patient any trouble but was removed because of the fear of its having contributed to an optic neuritis which had completely destroyed the sight of this patient's eye. This culture, as previously stated, was used for this test because of its high virulence. There was, however, an unfortunate phase of the selection of this particular culture, which was that since there would be some reason to fear that it would have an affinity for eye tissues, since that was the serious lesion from which the patient had suffered, we might confuse elective localization qualities on the part of the organisms with elective localization qualities of the defensive chemical injected. It so happens that one of these drugs—namely, ethylhydrocupreinhydrochlorate—has been suspected of producing injurious effects on the eyes of patients that were injected with it as a means of increasing their defense against the pneumococcus in cases of severe pneumonia. There is, however, a strongly expressed difference of opinion as to whether such injurious effects had been produced by this drug, or whether they were incidental or of other cause. In our rabbits inoculated with this culture, which was suspected to have had an elective localization for eye tissue, there was no opportunity for eye involvement to develop, since the animals were practically all dead inside of a day, only one living beyond that period, and it received an exceedingly small dose. Before this drug is used on humans as a means of reinforcing their defense against streptococcal infections, it is exceedingly important that extended researches be conducted to establish whether or not there is a danger of producing injuries to the eyes from its use. Several of the rabbits that received this drug prior to their injection with the culture, and which rabbits apparently had their lives lengthened or saved by the use of this chemical, developed conjunctivitis, and it was impossible to decide whether the lesion had been produced by the chemical or by the culture. Since, however, none of the controls which received the chemical without the culture, developed eye involvement, though they lived for from twenty-nine to fifty-four days before being chloroformed, it seems probable that the eye lesions which did develop, were the result of elective localization qualities on the part of the organism rather than the specific effect of this chemical.

With regard to the chaulmugra compounds, I found great difficulty in securing suitable extracts or compounds, and I found it necessary to engage the services of a skilled pharmacologist to make for me special preparations for my studies. A number of preliminary studies were made by using the chaulmugra oil and resorcin or camphor, but a special sodium chaulmugrate proved to be the least irritating and most efficient. A group of rabbits, not shown in our charts, received various dosages to determine the quantity that would be lethal and the quantity that would be most efficacious. This is presented as a preliminary report and more extended and detailed information will be reported later.

It will be noted that, of this group, many of the rabbits with-

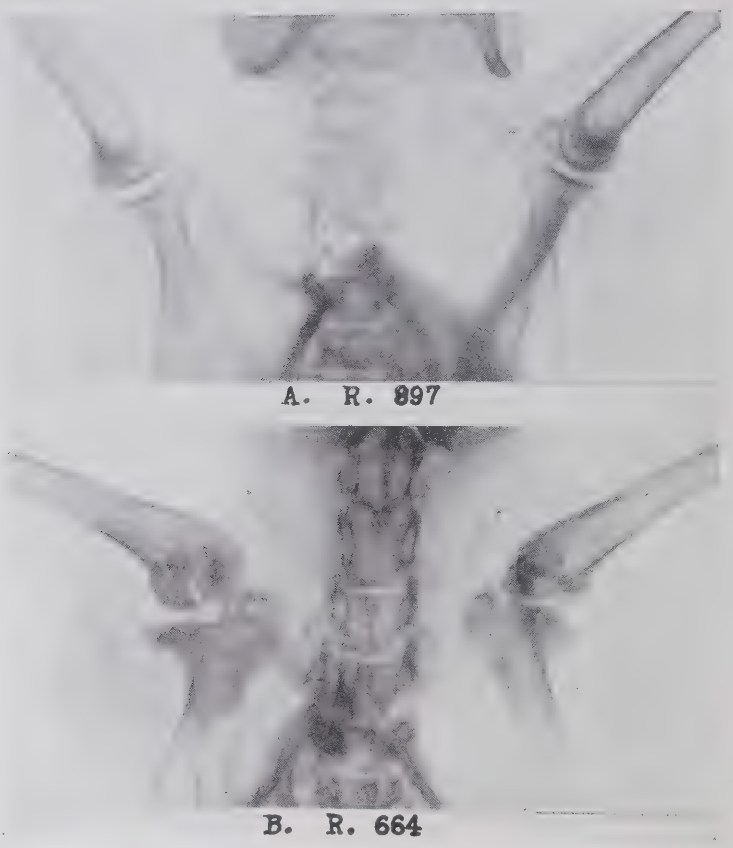

Figure 159. Proliferative arthritis shown in shoulders in B. A, normal; B, had received lethal doses of dental infection but had apparently survived because of the raising of its defense by chemotaxis.

stood the lethal doses and lived on for long periods, and were used finally to see whether the use of chaulmugra oil continued to give them defense. Rabbit No. 664 had the following history: The rabbit received four injections on four successive days with a culture, one of which injections was expected to be sufficient to kill an ordinary rabbit. It had been prepared by a previous inoculation with sodium chaulmugrate. It gained splendidly in weight and looked like a very normal rabbit. Its fur was sleek; and when posted, it was very fat, notwithstanding all of which, multiple arthritis was found, as shown in the roentgenograms in Figure 159. The roentgenograms of the shoulder joints of a normal rabbit are shown for comparison in the same figure in A. This would seem to suggest that, notwithstanding this animal was not able to prevent the localization of the organisms having an affinity for joints, it was able in large measure to resist the usual physical disturbances accompanying that process; for, notwithstanding its joints continually, though slowly, grew worse for six months, with a marked tissue change and accumulation of pus, it did not go into a state of decline with the characteristic decrease in weight which usually accompanies active rheumatic infection.

SUMMARY AND CONCLUSIONS.

There are several phases of this that must be kept in mind. First is the danger that may be done by injecting of such substances. This is particularly true of ethylhydrocupreinhydrochlorate, which may have a distinct injurious effect upon the eyes; and those who read this must be sure not to use it upon patients until much more work is done with it. The chaulmugra oil compound derivatives show promise of benefit. The experimental data are entirely inadequate as yet, however, to justify its use on patients.

> **These preliminary experiments would seem to suggest that, means can be developed which will effectually assist, by chemical means in the defense of the body against the invading streptococcal organisms of dental origin or from other sources which produce the rheumatic group lesions.**

CHAPTER XXVII.

THE EFFECT OF RADIATION ON DENTAL PATHOLOGICAL LESIONS.

PROBLEM: Can periodontoclasia and apical abscess and inflammation be cured by various types of radiation?

EXPERIMENTAL AND DISCUSSION.

We began our studies on this problem in 1897 and 1898, immediately after the announcement of the discovery of the Roentgen-rays and the acquisition of our first apparatus, which was one of the first west of New York City. These were followed by studies with radium before the name, "radium," had been given to it, and when the material from which the radium was finally isolated was called "Radio-active substance". I published a preliminary report on the former in The Archives of Electrology and Radiology, March, 1904[1]; and on the latter in the Dental Cosmos, May, 1901[16], read before the International Dental Congress in Paris in 1900.

The early forms of apparatus for developing Roentgen-rays, used tubes that were very soft and which operated on a potential represented by a spark gap ranging from a half inch to two inches. Many of these tubes required relatively long exposures because such a small percentage of the ray had sufficient penetration to reach the film, which was the reason for our early researches on the development of the triple-coated film which, if I am correctly informed, was the origin of the original Seed film which was later taken over by the Eastman Co.

We early discovered that when teeth with fistulae were subjected to the radiations from these tubes, the fistulae tended to close; that sore teeth became less sore. One of these incidents was about as follows: The patient was sent by a fellow-dentist for a roentgenogram of a tooth with a fistula which the dentist advised should be treated. After our several exposures, taking different angles, the fistula closed and the man refused to pay for the roentgenograms on the ground that they were not needed, that the tooth had cured itself. We, accordingly, established a series of investigations to determine what the effect might be on gingival infections as well as apical involvements when treated by this means. A series of special tubes with lead protectors was made to put into the mouth, generate the rays close to the tooth, and administer the dosage without raying other tissues. In our first group, we so treated a dozen and a half patients, about two-thirds of whom showed marked improvement when judged by the criteria of the flow of pus.

Enough data are available to demonstrate that we are dealing here with a force which, when it is understood, will doubtless be capable of lending great aid in the treatment of pathological conditions and, indeed, is already doing so in the treatment of neoplasms. We must, however, clearly distinguish between those changes from normal which develop in tissues as the clinical expression of the pathological involvement. In some instances we have a very markedly lowered capacity for reaction to irritation. Invaded tissues do not have the capacity for defending themselves against the parasitic intruder. Their very lack of vital reaction determines the outcome of the warfare immediately at the outset, for the condition must go from bad to worse, the organism gaining more and more vitality and virulence, as the tissue develops less and less capacity for defense. Clearly what this tissue needs is something that will boost and support its already too feeble capacity for reaction. This we will discuss presently. Over against this we have another type of reaction in tissue, in which the pathological state expresses itself with abundant cell proliferation and more than normal reactions, which process will include the neoplasms such as the various cancer growths and some stages of periodontoclasia, or pyorrhea alveolaris.

When radium, then, is applied to a neoplasm such as an epithelioma, it depresses that vital capacity which expresses itself in cell proliferation, and, if the dosage is properly adjusted, this depression may be sufficient to restore this tissue approximately to normal, by destroying or depressing all cells having that exalted capacity. If, however, this same type of cell depressant is applied to tissue whose only safety lies in its capacity to exalt its activity to any needed extent to baffle and overcome the invading infection, it is like putting the brakes on a wagon which the overloaded horse is struggling with his most extreme effort to take over the grade. In other words, those forms of radiation, which tend definitely to depress vital function, must not be used to depress function where an exalted function is desirable.

The type of bacterial flora present in a periodontoclasia pocket will indicate very directly and definitely many qualities of the environment from which it is taken. To the trained eye familiar with the microscope the bacterial culture reveals very definitely the type of inflammatory process present. One of the greatest mistakes that has been made in the study of suppurative periodontoclasia, or pyorrhea alveolaris, has been to interpret the cessation of the development of so-called pus as a cure of the lesion; and this is one of the mistakes that I made in interpreting the clinical results produced by my treatment of cases of so-called pyorrhea alveolaris twenty years ago, as reported in The Archives of Electrology and Radiology, March, 1904 (The Treatment of Pyorrhea Alveolaris with the X-rays.). I mistook a depression of the tissues, as expressed by their capacity to produce an exudate, as a cure. There is no doubt that some of the conditions were definitely benefited, and others were definitely aggravated, by that same treatment, for they represented entirely different stages of a pathological process, one hyperactive cell reaction, in which cases were benefited, and the other, a chronic depressed reaction state, in which cases were, doubtless, not only not improved, but, probably, definitely injured.

To test this further, I have made a series of studies with the mercury vapor arc lamp, to determine its effect upon the clinical conditions, as interpreted in the light of our newer knowledge, with the result, that there seemed definite evidence of a depressing effect on cell reaction, which was beneficial in only those cases having an exalted reaction state, and was definitely harmful in those cases with a depressed reaction state. To test this further, we placed teeth under the skins of rabbits and exposed the tissue over the implanted tooth to the quartz mercury vapor lamp. In every instance the animals died more quickly with this treatment plus the infected tooth, than with the same infected tooth without the mercury vapor lamp radiation; and, furthermore, we found that, whereas, when the rabbits died from the presence of the infected tooth alone, there was found all about the tooth an exudate carrying an abundant quantity of leucocytes; but when the rabbit was exposed to the radiation for fifteen minutes a day as we had been exposing our patients, there was found about the tooth practically a pure culture of streptococci with exceedingly few leucocytes; and, furthermore, when rabbits were exposed to the radiation without the presence of the infected tooth, we found that the radiation produced a definite depression of the leucocytes of the blood.

These studies strongly urge the establishment of researches which will adequately determine, first the reaction effects of the rays of various angstrom units, and second, a very careful differentiation between an exalted and a depressed cell activity in the various pathological states with which we are concerned. It would seem most unwise that routine clinical application should be undertaken before these fundamental problems shall be worked out. Some phases of this question will be discussed in the next chapter.

I have undertaken to apply rays of an angstrom unit between 300 and 1200 from mercury vapor arc in the treatment of periodontoclasia. One of the cases selected is shown roentgenographically in Figure 160. This was a case of chronic periodontoclasia, with much destruction of tissue and loosening of the teeth. The method of determining the presence or absence of improvement was by testing the hydrogen-ion concentration of the saliva, the bacterial types, and the quantity of their growth in the pockets, and the tightening of the teeth, with the improvement in the appearance of the gingival tissue. As judged by these criteria, there was but slight, if any, improvement; and, particularly, when judged by the bacterial flora, which is one of the best indications. In the second view in B, flexible gutta-percha points are placed in the pockets between the teeth; and the advantage of their use is very apparent, for it will be noted that in A the pocket between the two molars does not appear to be nearly as deep as it is shown to be by the passage of the flexible points, which stresses

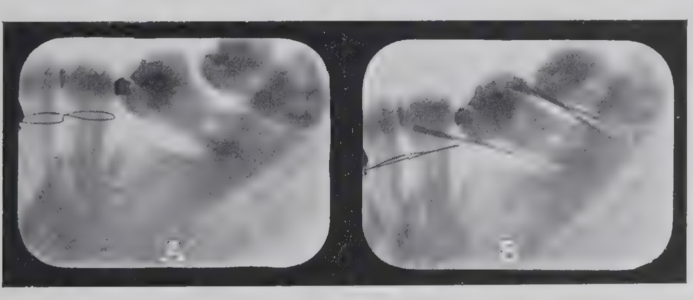

FIGURE 160. A CASE OF PERIODONTOCLASIA TREATED WITH ULTRA-VIOLET RAYS FROM A QUARTZ MERCURY VAPOR ARC. A, IS WITHOUT GUTTA-PERCHA POINTS IN POCKETS, AND B WITH. NOTE HOW DECEIVING A IS.

what so many have learned to their chagrin, that the conditions were very much worse than they were supposed to be, when judged simply by the roentgenogram. The dosage given was fifteen minutes with a quartz applicator, twice a week, for about ten weeks. If improvement would not be produced in that time, the treatment would not justify its continuance in our judgment. The slight improvement in the types of bacterial flora was temporary and tended to return to its former type quite early after the cessation of the treatment.

In order to determine more exactly what the effect of such treatment would be, I placed an infected tooth beneath the skin of a rabbit, and treated same with the quartz mercury vapor arc lamp by flooding the tissues over where the tooth was planted beneath the skin, with these rays for fifteen minutes a day for two days, the day of the implantation and the day following. On the third day it was chloroformed. It was our belief that the tissue broke down more rapidly, and tissues became a prey to the infection more speedily, than when this tooth and other teeth were planted beneath the skins of other rabbits. There was also a very marked decrease in the number of leucocytes present in the fluid surrounding the infected tooth. The rabbit was posted on the third day, at which time it had lost 130 grams, or 10 per cent, and showed at necropsy, subcutaneous gangrenous necrosis, with edema of the underlying tissues. There was marked hyperemia of the thyroid, spleen, and kidneys.

I, therefore, decided to make observations on the effect of these radiations on a normal rabbit. Its blood was studied prior to its exposure to the rays and then frequently observed during the treatment. Results are shown in Figure 161, which records the various elements from day to day. It will be noted that there was

EFFECT OF RADIATIONS ON BLOOD OF NORMAL RABBIT

Date	Hemoglobin	Erythrocytes	Leucocytes	Polynuclears	Lymphocytes		Basophiles	Mononuclears
					Large	Small		
*3- 8-23	85	7,000,000	7,200	**59**	8	**24**	1	8
*3- 9-23	85	4,300,000	10,800	**64**	16	**17**		3
3-10-23	85	4,550,000	7,800	**53**	12	**26**	2	7
3-12-23	80	4,770,000	4,600	**40**	11	**43**	2	4
*3-14-23	85	5,150,000	6,000	**36**	8	**55**		1
*3-15-23	85	5,650,000	9,900	**35**	8	**54**	1	2
*3-19-23	80	5,800,000	5,400	**43**	6	**50**		1
3-23-23	80	5,050,000	7,800	**41**	11	**46**	2	

* The rabbit received 15 minute treatments following the blood counts

FIGURE 161.

a decrease in the percentage of polymorphonuclear cells, with a marked increase in the small lymphocytes. In our studies with infected teeth planted beneath the skins of rabbits, and when cultures are inoculated of dental origin, there often develops a decrease in polymorphonuclears and an increase of lymphocytes as part of a developing leucopenia, which depression of leucocytes always indicates a poor defense progressing toward death, which usually cuts short the experiment in a few days after its development. A very important effect of the radiation on this rabbit is expressed in the change in ionic calcium of the blood, as shown in Figure 162. On the 8th, this was 10.4 mgs. per 100 cc., approximately normal. The first reaction to the stimulation of a single exposure increased the ionic calcium to 11.13; and on the 13th, this had changed to a distinct pathological state of 8.27. Another very striking feature of this change relates directly to calcium metabolism; for the combined calcium of the blood on the 8th was 1.7; on the 9th, it had increased to 3.7; and on the 13th, to .5.

EFFECT OF RADIATIONS ON BLOOD CALCIUM OF NORMAL RABBIT

Date	Calcium plus Thrombin	Thrombin Equivalent	Calcium Ionic	Calcium plus Combined	Combined Calcium
3–8–23	17.60	7.199	**10.401**	12.13	1.729
3–9–23	19.00	7.866	**11.134**	14.878	3.744
3–13–23	17.20	8.923	**8.277**	8.793	.516

FIGURE 162.

I have made a number of studies with radium, and have found it very difficult to be sure that I was properly interpreting the results because of the difficulty of knowing the proper dosage, for just as a little strychnine may be good, and a very little more may be very harmful, just so a proper dosage of radium or otherwise, may be distinctly beneficial, and just a little more distinctly harmful. I am, therefore, withholding these studies until I have more data, for it is exceedingly difficult properly to control and limit the effects of radiation to the pathological tissue, it being so intimately related, anatomically, to normal tissue; and the very treatment which may be a benefit to the former, may, at the same time, be harmful to the latter. If we put a medication into a pocket of periodontoclasia, its action may be quite completely limited to the tissues with which it comes in contact and those very closely adjacent. Radiations, on the contrary, pass not only through the adjacent tissue, but through the entire body in many instances, and the dosage and application are not within easy control. For this reason we have undertaken to use the radiations from silver chloride in colloidal suspension but, while these have bactericidal effects, and will even pass through a glass tube, we have not found that placing either the tooth containing a tube of this material, or the tooth saturated with it, was sufficiently less harmful, when planted beneath the skin, to assure us that it was an efficient germicide. It is a favorable field, however, for investigation.

There are many reasons to believe that great benefit will ultimately come from an adequately intelligent use of radiations of various lengths, when properly selected and adapted to the needs required. We now know that neoplasms represent a diverted cell function, which, in the proliferative types, express an overactive state; and any force which tends to depress, will thereby suppress the proliferation. For this the very short rays of the x-ray and radium tube are most efficient. Similarly, we know that radiations of the range of three hundred to six hundred tend to produce beneficial changes in rickety conditions; and again, we know that whereas animals will die of vitamin deficiency when fed on dried peas, for example, they will be promptly restored by being fed on these same dried peas that have been allowed to sprout and been exposed to sunlight. Similarly, the algae of the sea, through their exposure to the sun's rays, have become immense storehouses for vitamins, which latter are stored in the livers of the fish, and hence are largely in use, medicinally, in cod liver oil. It is also general knowledge that sunlight is necessary for health. The rickety children in a smoky city will recover by being moved to the sunlight of the clear country, even though retained on the same diet. Not only is this true, but just as the distance from the equator is lengthened, mankind is required to use more of the vitamin storage foods as he approaches the shorter days and hence decreased sunlight, which is the reason that Labradorians and Arctic inhabitants live so much on the fats and oils of fish.

When we come to know the true nature of disfunctions of various tissues and organs, we can then judge wisely what type of ray should be used to improve its condition, and interpret wisely what constitutes an improvement and what an apparent improvement but an actual injury. An illustration of the latter can clearly be seen in the misconception regarding the significance of a closing of a dental fistula after exposure to Roentgen-ray, and the cessation of the so-called pus from periodontoclasia from exposure to Roentgen-ray and other radiations. I am not decrying these means, but I am trying to point out that we must understand their fundamental pathology before we can treat them intelligently or interpret wisely the results of our efforts. This, therefore, is a field that represents a crying need for exhaustive research on the basis that will be competent to bring about dependable and properly interpreted results.

CONCLUSIONS

The results of these studies suggest to me the following:

(1.) That these three forms of radiation—namely, Roentgen-ray, radium radiation, and ultraviolet as generated from mercury vapor and quartz tube—have definite effect on cell resistance to proliferation, and thus directly upon tissue reaction expressions such as pus, bacterial invasion, and granulation.

(2.) That some of these forces are, apparently, definitely harmful; that others are, apparently, definitely helpful.

Our interpretations of these phenomena are given in Chapters 45 to 56.

CHAPTER XXVIII.

GINGIVAL INFECTIONS, THEIR PATHOLOGY AND SIGNIFICANCE.

PROBLEM: Are the present theories regarding the etiology of periodontoclasia, or so-called pyorrhea alveolaris, correct?

EXPERIMENTAL AND DISCUSSION.

I cannot find in all of medicine, whether in general medicine or in the specialties including that of dental medicine, instances of very common diseases which have so completely baffled explanation or which contain so many paradoxes as has this disease. In the minds of the majority of the members of the dental and medical professions, and as well, and naturally so, in the minds of the members of the laity, this disease is thought of largely as a true infection process. The imperative necessity for brevity in these reports precludes the possibility of presenting, herewith, a history of the theories as to its etiology. For such, I would refer to various books on general or dental pathology.

Lately, it has come to be recognized and thought that irritants play an important part, and that their removal becomes a fundamental part of the treatment of this disease, though their removal does not explain its etiology. Similarly, traumatic occlusion has come to be recognized as an irritant and, like a foreign substance, must be corrected. One of the advanced thinkers in the etiology of this disease, Eugene Talbot, has advocated that the supporting structures of the teeth are transient tissues and, as such, tend readily to be absorbed, which accounts for the fact that, in the presence of bacterial invasion and irritation, that process which is part of senility, sets in early. In his paper entitled "The Etiology and Treatment of Interstitial Gingivitis,"[16] he states:

"When we consider the peculiar endotransitory nature of the alveolar process, degeneration of tissue is the natural result. At the senile period when the excretory organs are diminishing in activity and in disease, vital resistance is at its lowest ebb, metabolism is diminished, and degeneration and absorption of the alveolar process is in active operation. As age advances, the destruction of bone is a natural normal pathologic process".

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[16] See bibliography.

About twenty-five years ago, I started a quite intensive study of this disease, and found that every time I approached the problem through the doorways of the available theories, I ran into a network of contradictions and confusions which persuaded me that there were some things fundamental, of which we were not as yet appraised, and which were the most important factors in the etiology of this disease. And since the workers in this field had apparently not succeeded by approaching from the regulation doorways, I decided to make a new approach—namely, by way of an exhaustive analysis of the clinical data and a careful examination of the characteristics of the individuals presenting with that affection, and relating these data to the blood and saliva chemistry and bacteriology. Accordingly, as a part of the susceptibility study to streptococcal infections, we have carried on an extensive study of the characteristics of all individuals with regard to their susceptibility to gingival and alveolar infections. There soon appeared in these studies, either a great anomaly or a great truth. For a long time we could not accept it as a fundamental truth; it was so paradoxical to the conception we had entertained.

In discussing the clinical phase of this group of affections, I have presented much data which are necessary for our approach here, and to save repetition, I will refer back to those chapters for many references These are found particularly in Chapters 4, 8, and 10.

Figure No. 44 shows the result of a series of studies that was made several years ago, and tabulated three years ago, which showed that, when patients with or without susceptibility to rheumatic group lesions, were divided into progressive groups in accordance with the degree of that susceptibility, a very important change took place with regard to their susceptibility to periodontoclasia. In Group No. 1, absent susceptibility, the percentage with periodontoclasia was 23; Group No. 2, acquired susceptibility, 33%; Group No. 3, very mildly inherited susceptibility, 25%; Group No. 4, moderately strong inherited susceptibility, 0%; and Group No. 5, very strong inherited susceptibility, 0%;whereas, in these various groups extensive caries was as follows: Absent susceptibility, 51%; acquired susceptibility, 91%; mild inherited susceptibility, 81%; moderately strong inherited susceptibility, 88%; and very strong inherited susceptibility, 100%; and the presence of locked dental infection tended to increase from 58% absent susceptibility, 75% acquired susceptibility, 44% mildly inherited susceptibility, 75% moderately strongly inherited susceptibility, to 86% very strongly inherited susceptibility.

In order that we might thoroughly check so great a new truth, if such it be, before presenting it, and with the most earnest desire not to permit an error to be presented, we have refrained for several years from announcing this important discovery, awaiting a satisfactory mass of data that would either establish or disprove it. Accordingly, a new corps of assistants has tabulated a new group of findings, not knowing either the results of the former studies in this regard, or even that they had been made. These results are shown in Figure 85 of Chapter 10, the latter chart giving as follows: Absent susceptibility 40; acquired 33; inherited one side mild 33; two sides mild 20; one side strong 20; two sides strong 0.

This was further shown in Figure 87 which reveals that, when individuals are divided into three groups—absent, acquired, and inherited (the latter of all grades of inheritance)—, the percentage of individuals affected with periodontoclasia in the group recorded as absent susceptibility was 48; acquired susceptibility 29; and inherited susceptibility 16.

All observing dental clinicians have noted for decades that teeth with extensive gingival infection do not suffer carious destruction. This paradox seems to hold an important key to the interpretation of much of dental pathology.

An extensive study of the bacterial flora found in periodontoclasia infections has demonstrated that there has been a great divergence of opinion as to the causative invading organisms. Of the workers, Hartzell and Hendersy have stressed the importance of streptococci, while most workers, both early and late, have noted the presence of spirochetes and fusiform. The great drawback in the study of this disease has been found in the fact that the characteristic bacterial growth cannot be produced in artificial media. Some of the workers have been able to grow a few of the organisms. Our studies have shown a quite definite tendency to grouping of bacterial types of infection: those in which fusiform and spirochæte abound almost exclusively; those in which spirochæte abound almostly exclusively; and those where these two types are very scarce, if not almost entirely absent, with an abundance of short rods, staphylococci, streptococci.

In order to determine the significance of the important data revealed in the relationships between gingival infections and the other outstanding clinical conditions—namely, presence or absence of dental caries, presence or absence of systemic involvement, types of local dental pathology—we have related each of these conditions as found in various individuals to the serological and chemical changes in the blood, saliva, urine, etc., of those individuals.

In Figure 85, Chapter 10, I have shown that tendency to gingival infection is, in large measure, in proportion to defensive activity, and, therefore, in proportion to absence of rheumatic group lesions, these figures progressing from 40 per cent of the individuals with absent susceptibility having periodontoclasial processes, 33 per cent of the acquired group, 33 per cent inherited one side mild, 20 per cent inherited two sides mild, 20 per cent inherited one side strong, and 0 per cent inherited two sides strong. I do not present these figures with any thought that they are exact, but, when taken from such a large number of cases and from several groups by different individuals, the fact that the result is, in general, constant, suggests that they are relatively correct. We do not yet know the significance of many of the new data that we are here presenting, but it is a matter of exceeding interest and of undoubted importance, that patients with active periodontoclasia without exception, in our experience, have been found to have a high ionic calcium, in the order of 11 to 12.5 mgs. per 100 cc. of blood, as compared with 10 to 10.5 for our accepted normals.

An analysis of this clinical data reveals the remarkable fact that in some way the presence of an active defense against streptococcal infections, in so far as the absence of rheumatic group lesions is concerned, is directly related to the clinical expression which we find as periodontoclasia, or pyorrhea alveolaris, *in certain of its stages.* It is not an accident that so many people with such extensive gingival suppurative processes are apparently in excellent health.

For determining the factors involved in the lesion known as periodontoclasia, or pyorrhea alveolaris, we have undertaken to discover the contributing influence of each. An analysis of these suggests that mechanical irritation, bacterial invasion, and defensive reaction, all play important parts. In order to determine the relative importance of all of these we have treated different groups in different ways. In the first group no other means has been used than the mechanical removal of irritation; in the second group no other means than local bactericidal treatment; in the third group systemic bactericidal treatment; in the fourth group the changes in the peridental tissues where the individual's defense had been lowered by inflammatory and other causes; the fifth group artificial stimulation of gingival tissues. These showed as follows: That in the early stages of periodontoclasia the simple elimination of the substances producing mechanical irritation, thus removing the primary irritant which caused the inflammatory reaction, entirely removed the periodontoclasia, or pyorrhea alveolaris. In the far advanced conditions the removal of the mechanical irritant made much less improvement, and in some cases very little. In the series of cases studied to show the effect of local bactericidal treatment we have many illustrations which reveal a marked improvement in the clinical conditions with no other treatment. The effect of systemic bactericidal treatment, in which case the injection of emetin and succinimid of mercury was used, showed marked improvement in local clinical symptoms even though the mechanical irritant was not disturbed.

Another series of studies was very illuminating. These were conducted in 1898 to 1904 on the use of the Roentgen-ray in the treatment of periodontoclasia, which we have discussed in the preceding chapter and which was published in The Archives of Electrology and Radiology, March, 1904.[1] In those studies I found that Roentgen radiations tended to depress the reaction capacity of the tissue to a marked extent.

Inasmuch as the local bactericidal treatment and the mechanical removal of the irritants each produced practically complete removal of the local oral symptoms, it suggested very strongly the great need for a research upon the problem of the improvement of germicidal procedure. For this purpose a series of researches has been carried on for several years, at one time taking practically the entire time of a trained bacteriologist for one year, to ascertain the drugs and chemicals that were most efficient in depressing the type of bacterial growth which tends to develop

[1] See bibliography.

in the mouth, in which there is a marked susceptibility to development of periodontoclasia, or pyorrhea alveolaris. These researches themselves would fill a volume and will only be summarized here to present the important results. Their application is made in extended detail in a later presentation.

The following types of drugs were found most efficient, though some were not suitable because of undesirable qualities: Mercuric nitrate (This discolors the teeth in time and has the possibility of systemic irritation.); chaulmugra compounds; chlorine compounds; zinc compounds, particularly the chloride and sulphocarbolate; silver compounds.

In the group of individuals studied by mechanical stimulation of gingival tissues, a very marked change in the local clinical conditions was shown. With the improvement of the circulation, there was a marked decrease in both the bacterial growth and development of exudate and also in the hypertrophy and congestion, notwithstanding the fact that the massage was done against tissues, which were being pressed against rough deposits on the necks of the teeth, the effect of which was to lacerate and injure these tissues. Notwithstanding this latter fact, the improvement was very marked.

Since it is demonstrated that marked beneficial results may be secured by each and all of the methods of procedure, though some more than others, it becomes apparent that the utilization of those means, which are most easily applied, will in many cases be all that is necessary to prevent the development of this clinical condition. This involves first the mechanical removal of irritation; second, the use of bactericidal means for depressing the type of organisms which develop in this condition; third, the use of mechanical stimulation to prevent the passage of those fluids which tend to nourish the bacteria from the surrounding tissue into the pockets of periodontoclasia and to provide the rapid exchange of fluid in the involved vascularized tissues in order to bring new defensive factors and carry away waste products, the use of substances producing radiation in order to reduce to normal the reaction capacity of the tissue exalted as a part of the infective process.

In the chapters on Tooth Medication, Radiation, and Chemotaxis, I have reviewed the effects of the use of substances producing radiation for reducing bacterial growth and exalted tissue reaction. In a later presentation I will give special formulas for the development of tooth powders and methods for their use, suited to each of the different types of extreme oral conditions, such as tendency to caries, tendency to gingivitis, periodontoclasia, pyorrhea alveolaris, etc. These are so simple that they may be put up by any good druggist and should be available to humanity at small cost; and if used sufficiently intelligently and faithfully as indicated, will almost completely prevent the development of the disease known as periodontoclasia or pyorrhea alveolaris.

It is most important that we urge the reader to keep in mind a very great difference in the type of gingival infection which is typical of the active suppurative type in its early stages, which responds readily to the removal of local irritants and to stimulation, from the chronic non-suppurative poorly reacting condition. In this discussion we are referring distinctly to the early active process which has an entirely different pathology from the other types which represent the ravages of the former active processes, carrying it over into a changed systemic condition.

When we relate the following factors—namely, the relative extent of absorption of supporting structures, whether apical or gingival, the presence or absence of systemic involvements, the absence or presence of dental caries, the ionic calcium of the blood, the ionic calcium of the saliva, the alkali reserve of the blood, the alkali reserve of the saliva, the uric acid content of the saliva, the uric acid content of the blood, urea nitrogen of the saliva, urea nitrogen of the blood,—we find certain groups of conditions are, practically, invariably associated. The individual with the high defense has a normal ionic calcium of both blood and saliva. It is apparent, then, that this quality of the presence or absence of gingival infection with a given irritant is related directly to calcium metabolism. When we make a careful study of the characteristics of the various physical states which modify calcium metabolism most, we find that just in proportion as that individual is able to maintain a high or abnormally high ionic calcium balance of the blood, in that same proportion his gingival supporting tissues tend to be absorbed easily in the presence of irritation.

This research has been planned to establish, if possible, what some of the direct variable factors are in connection with this susceptibility to destruction of the alveolar bone in these cases. A careful study of the saliva reveals, and that readily, that it is more alkaline in individuals with a marked tendency to periodontoclasia. A more exact study of the hydrogen ion concentration of the contents of the pockets of periodontoclasia shows that in the active condition it is very alkaline, reaching as high as 7.7 whereas the hydrogen ion concentration of the blood is 7.3.

In another chapter we have noted the important clinical fact that the sockets of extracted teeth, which teeth were involved with acute periodontoclasia, tend to heal with great ease and rapidity, seldom requiring a treatment following the extraction. A blood clot is readily formed. It is well organized. It becomes vascularized by the development of embryonic blood vessels in the clot, and its socket heals without pain and without the clot's ever breaking down; whereas, on the other hand, a socket of a tooth with marked condensing osteitis without a tendency to involvement tends to have its blood clot break down, readily becomes painful, and in many cases develops what is clinically termed "dry socket", which condition is characteristic. An analysis of the saliva of this type of patient shows a lower degree of alkali reserve; his blood shows a lower ionic calcium; and, immediately, we are dealing with two distinct types of individuals. This problem of the postoperative treatment of the sockets of various types of individuals will be discussed in a later presentation.

A careful microscopic examination of the contents of these two different types of sockets has revealed an important new group of facts, which are so constant, that they become immediately definitely diagnostic. The leucocyte found in the socket of the tooth extracted with periodontoclasia is largely a polymorphonuclear with several lobes. The cytoplasm is filled with granules which are readily disclosed either by the dark field or direct illumination, and with certain types of vital stains; but most important, these polymorphonuclears show a rapid motility of these granules. Many of these cells contain bacteria which are in relatively small quantities outside the leucocyte, in proportion to the clinical picture found in the other type of socket, which latter, in contrast to the former, has few leucocytes with actively motile granules, relatively few phagocyting leucocytes, and larger numbers of organisms outside these cells.

We have, then, a direct measure in this process of the activity, and since a socket shows, under treatment, these highly active granular polymorphonuclears, it usually goes on readily and rapidly to complete healing process. So far as we know, this phenomenon has never been reported. We have not been able to find a reference to it in any literature or by correspondence with our leading hematologists.

A closer study reveals that, if in a socket of the second type—namely, without the presence of this large number of characteristic granular leucocytes whose granules are highly motile—we place an ionic calcium, as, for example, calcium chloride together with bicarbonate of soda, within a few hours the pain subsides, the type of leucocyte changes, and the type of socket has been changed so that it starts immediately on the process of repair. This has led us to a careful analysis of the relationship between the process of decalcification and ionic concentration of calcium, and these in relation to the alkali reserve of the blood.

A further analysis of the various charts in which we have compared the clinical expressions, structural changes, and chemical analyses, we find that in those cases where the suppurative process was most active, the content of the pockets of periodontoclasia were most alkaline, the ionic calcium of the blood high normal or above normal, blood sugar higher than normal, trabecular differentiation of alveolar bone very marked, caries low or zero, tissue repairing qualities excellent, inflammatory response to mechanical irritation acute, etc., all existing in an individual with every evidence of a high defense to rheumatic group lesions such as complete absence of heart involvement and rheumatism. In sharp contrast to the preceding, we find that the individual who has a marked susceptibility to rheumatic group lesions strongly tends not to have pockets of periodontoclasia even in the presence of irritation sufficient to produce same, such as gold crowns, food packs, etc. In him the ionic calcium of the blood is below normal, blood sugar not above normal, trabecular differentiation diffuse and not marked, caries high, tissue repairing qualities—particularly of alveolar bone—poor, inflammatory response to mechanical irritation subacute or low, etc.

This relationship between the clinical, serological, and chemical factors, has suggested to me that these must be related as cause and effect; and, accordingly, a series of researches is being made to ascertain, if possible, the mechanism of this reaction. We are, accordingly, taking a large group of extreme cases of each of the different types and carrying out these studies in further detail with especial reference to the relationships between the alkali reserve of the blood and the clinical symptoms, such as the destruction of the gingivæ, the peridental membrane, and the alveolar bone.

From these data it is shown that as the alkali reserve goes down and the ionic calcium goes up, there is a marked tendency to acute inflammatory reaction to irritations, with necrosis of soft tissues, and absorption of alveolar bone; and where the alkali reserve is not below normal and the ionic calcium not up to normal, there is not marked reaction to irritation of gingival tissues and but little absorption of alveolar bone. In Chapter 44 I have discussed the relationships involved in these phenomena in detail. It is there shown that one of the system's most difficult and exacting operations is the maintenance of the normal hydrogen ion potential of the blood, which is made possible only by an ample reserve of buffers to take care of sudden increases in acidity or alkalinity, particularly the former, called the alkali reserve of the blood. For ordinary purposes in normal individuals this can readily be done by drawing upon the compounds within the blood itself together with respiration. This becomes increasingly difficult as that alkali reserve is reduced; and since the mechanism of defense is made very active, doubtless by hormones, but also very largely by a high ionic calcium of the blood, catabolic and physiologic processes are carried out with great ease and rapidity. For the process of defense against infection, Nature has provided the flooding of the parts with an alkaline plasma. The mechanism is available to create the alkalinity of the fluids bathing the parts in periodontoclasia, but the reserve supply of buffers is so greatly reduced, that Nature must resort to other sources of material for producing this alkaline medium. She, accordingly, must have some means for producing an alkaline medium in the absence of a low alkali reserve in the blood. In order to determine this reaction we have carried out the following research:

Since the hydroxyl ion is increased in the saliva of individuals with a marked susceptibility to periodontoclasia, it should be possible to determine what substances have taken part in that process by comparing the concentration of the various constituents in pockets of periodontoclasia and in the saliva itself, the latter furnishing the medium surrounding the environment, the former a mixture of the latter with the products of the reaction within the pocket. To determine this I have made a series of studies in which we have compared the following elements in the pockets of periodontoclasia and in the mixed saliva of the mouth and compared them with the blood chemistry. Since the blood and saliva must largely furnish the constituents for the pocket of periodontoclasia, it immediately becomes apparent that any marked increase in any element found in the pocket of periodontoclasia over that of the blood and saliva will indicate that there has been some other source. These have shown that the total calcium of the pocket of periodontoclasia is much in excess of that of either the blood or saliva. This cannot be accounted for on the basis of concentration. It will be noted that as the OH ion increases in the production of alkalinity, there is an increase in the excess of calcium over that of either the saliva or blood. There is also an increase in the phosphorus. This immediately suggests the question, Where do these substances come from to make this excess? When we compare the relationship between the calcium and phosphorus of the saliva with those elements in the blood of individuals without periodontoclasia, we find that it is not normal for those substances to appear in the saliva in greater concentration than their existence in the blood, and that their concentration increases as the clinical expression of periodontoclasia. It is, therefore, apparent that this alkalinity is accomplished by an increased cell activity with an osteolysis partly the result of the increased concentration of calcium ions, which activity has torn down the alveolar structure to secure neutral calcium phosphate in the absence of the normal alkali buffers of the blood, whose normal function would be to supply this demand.

It frequently occurs that patients with profuse spirochete infections, are suffering from marked toxemia, with progressive loss of weight. A typical illustration of such a case is shown in Figure 186 of Chapter 35. This patient had lost eighteen pounds in weight in three weeks; and immediately following the treatment of his gums, the patient gained ten pounds in two weeks.

Since the preceding researches on the etiology of periodontoclasia, or so-called pyorrhea alveolaris, have demonstrated the important role of each alkali reserve of the blood, alkali reserve of the saliva, ionic calcium of the blood and ionic calcium of the saliva, it is important to determine, if possible, some of the mechanisms of the contributing factors to this process. Our microscopic studies referred to have revealed the presence of large numbers of a type of polymorphonuclear containing very actively motile granules. This leucocyte is also very abundant in the sockets of extracted teeth which are repairing rapidly and satisfactorily, but greatly diminished or absent in sockets healing slowly or with pain or necrosis of tissue. As stated previously, it seems certain that these cells play a very important part, since they are present in both these conditions which represent in a sense opposing states, for one is rapid repair and building up of tissue, and the other is the tearing down of tissue. The same socket, from which the tooth with periodontoclasia is removed without any treatment whatever, practically always heals with exceeding rapidity and practically always without pain, necrosis, or infection. The placing of a foreign irritant, such as a piece of metal, in this same tissue does not produce the same type of reaction, either as expressed in exudate or tissue change, as does the presence of this type of tooth, mere removal of which completely reverses, or at least modifies, cell activity.

Normal adult tissue does not tend to proliferate after an organ or structure has reached its normal size. During the growing period, all tissues tend to multiply at a physiological rate constituting growth, which process is progressively slower with age until the adult development is reached. It is as though an arrow were shot from a bow, or a bullet fired from a gun. Each has its maximum velocity at the beginning of the flight. The velocity slackens at a definite rate; the period of rest is reached. In normal tissues there is no tendency to take up the condition of proliferation until conditions become abnormal. If tissue be injured, there is an immediate reaction in the local circulation, the capillaries distend, leucocytes come to the parts in large numbers, plasma exudes, and in proportion to the extent of the injury the reaction may include the entire body of the organism. White connective tissue cells rapidly begin to multiply; embryonic blood vessels extend from the capillaries; and after a clot has been formed and is not infected, this vascularization and rapid tissue generation extends into and throughout the clot. Finally, the tissues are rebuilt, proliferation ceases, rapidly formed connective tissue will be slowly rebuilt with the normal type of tissue of the part, and again Nature settles down to her normal, and there is no more cell proliferation.

This same process takes place when a tooth is extracted from a normal individual and is precisely the procedure with the repair of the socket after the extraction of the tooth. This, however, does not occur in those individuals with a low calcium and with a marked susceptibility to rheumatic group disturbances. This is doubtless partly occasioned by the fact that, the tissue, which has to take part in the repair, is distinctly different in the two types of individuals. In those with high defense there is little sclerosed bone, the medullary spaces between the trabeculæ are normal in size, and the alveolar bone is well vascularized. We have shown from our clinical studies that, one of the most conspicuous differences between these two types in their healing process, is in the absence in the latter, and the presence in the former, of a particular type of leucocyte, a polymorphonuclear with highly motile granules.

SUMMARY AND CONCLUSIONS.

From these data we are led to conclude: First, that the fundamental factor in periodontoclasia, or pyorrhea alveolaris, is not a specific infection; second, its etiology is in a direct way related to the presence or absence of susceptibility, by both being symptoms of a definite systemic condition; and third, the disease we have known as periodontoclasia, or pyorrhea alveolaris, is in some very definite way related to defensive factors. Since all of these researches combine together to furnish the new interpretation, it becomes necessary to reserve that interpretation for the chapters assigned to that important part of this presentation. It will be found in Chapters 45 to 56.

We would briefly summarize our interpretation of these data as follows:

> (1) **Inflammatory processes of the tissues about the teeth are a direct expression, and therefore a measure of the vital capacity for reaction of that individual to an irritant, during those stages of these lesions, characterized by an abnormally high vital reaction.**
>
> (2) **The individual, who has had this capacity for a very active reaction to the presence of irritants, may pass into a condition or state in which he or she has lost that high defensive factor, at which time several changes develop including a cessation of the absorption of alveolar bone, a lowering of the alkalinity of the periodontoclasia pockets, a change in their bacterial flora, all of which may provide under these later conditions a focus for systemic infection of the most danger-**

ous type, though they may have ceased either to have evidence of local inflammatory disturbance, or exudate as pus.

(3) To the ordinary observer, lay or professional, these two very dissimilar states are considered to be similar or identical though they are potentially very different.

(4) These different peridental expressions or reactions to irritations are accompanied by, and doubtless related to, changes in the ionic calcium of the blood.

CHAPTER XXIX.

ETIOLOGICAL FACTORS IN DENTAL CARIES.

PROBLEM: What are the dominant etiological factors in dental caries?

INTRODUCTION AND DISCUSSION

We have seen from the foregoing chapters, the following very outstanding data regarding the conditions associated with the presence and absence of dental caries: First, individuals with a marked susceptibility to dental caries have at that time an increased susceptibility to rheumatic group affections, and this group tends in this condition to have a depressed ionic calcium of the blood; second, individuals without susceptibility to dental caries and with a susceptibility to periodontoclasia (pyorrhea alveolaris) tend not to be susceptible in this condition to rheumatic group lesions and tend to have an ionic calcium of the blood, normal or above; third, this latter group does not tend to have dental caries.

It seems, therefore, very probable that susceptibility to dental caries is linked very closely and directly with the calcium factor of the blood and saliva. To determine this, we have made a large number of both total and ionic calcium determinations of saliva and blood of individuals with and without dental caries. A careful clinical examination of these individuals reveals that the saliva in the mouths of the patients with the periodontoclasia (pyorrhea alveolaris) tends to be markedly on the alkaline side of neutrality, with an increase in alkalinity in the periodontoclasia pockets. It is a conspicuous fact that dental caries never occurs in periodontoclasia pockets at the time of the active process.

(Active absorption processes may resemble caries but they constitute a different phenomenon.) It is a most remarkable fact that, in general, the efforts that have been made to produce artificial caries have either been only partially successful or entirely negative. It seems apparent that some very fundamental elements in the process have not been provided for.

With this in mind I have chosen to attack this problem from a new angle. Since all proteins and colloids are now shown to act probably, stoichiometrically—that is, by the purely chemical force of primary valency—we may assume that with a change of the hydrogen-ion concentration from the alkaline to the acid side of the iso-electric point of that medium, we will have a change in the ion of that medium with which that substance will enter into chemical combination. We are quite familiar with the illustrations of the charged ions from a silver electrode, which is positively charged, disbursing from that electrode with their positive charges under the law, that like potentials repel, and unlike potentials attract.

When a tooth is bathed in saliva with pH above the iso-electric point of that saliva, it can combine only with the anions, which are metals and bases; or, when of a pH below this iso-electric point, will combine only with acid ions. If, however, the entire tooth or the majority of its surface is bathed in saliva of a Ph above the iso-electric point and at some point on the tooth there is, because of mechanical conditions, a lower hydrogen-ion concentration sufficient to be on the acid side of the iso-electric point, immediately two distinct changes have been established. In this latter condition there is a reversed polarity with the result that the tooth surface will be positive, the liquid in this restricted acid zone negative, while the balance of the tooth will be negative to a zone which is positive: namely, the surrounding saliva. This establishes a closed circuit battery. As ions of calcium compound are dissolved by the acid, they are charged with the same sign as the tooth and therefore repelled from it; and with increasing concentration of that acidity there is an increasing repulsion of the calcium from the tooth, whereas the normal environment of the tooth should be alkaline and the tooth and the calcium should be of opposite charge, and the tooth would therefore attract the calcium ions and that would, by the process of crystallization, build into and upon the tooth structure, if that alkalinity became sufficiently strong to make the potential charge greater than the force required for the crystallization and ionization.

We have, then, the visualization of dental caries. The normal saliva is slightly on the alkaline side of the iso-electric point of saliva. The normal tendency is for calcium ions to have an opposite charge to that of the tooth structure and therefore will be attracted to it and the process of intensive calcification will go on by purely stoichiometrical processes, which must be recognized as slightly different from the metabolism, as we think of it, in cell function since there are no living cells present in this process.

Starches lodge in interstices of the teeth in which they are protected from the alkaline saliva in which, if not protected, they could not develop. Nor could the acid medium they generate remain acid if the normal saliva had free access to it to neutralize it. But proteins, such as the saliva, are amphoteric—that is, have the capacity of being either acid or alkaline—and this same saliva may be chemically very similar, except in relation to the compounds which will be built up and torn down by it, and from it. The lactic acid producing organisms, of which there are many, can in this environment produce a pH as low as 4 or even 3. This would make a marked difference of potential and completely reverse the forces between the tooth and the medium surrounding it. The organisms are, however, directly protected from the surrounding medium by an organized membrane, the bacterial plaque, which is a leathery substance, a result of chemical combination between an excretion of the organisms and the proteins of the saliva. As fast as these acid ions come through this membrane, they combine with the proteins of the saliva, producing substances which are insoluble in the saliva. The following factors are necessary for the maintaining of this condition. The alkali reserve of the saliva must be decreased, in general, to a point sufficient to make it possible for a still further lowering to be established and maintained at a point of bacterial protection of an acid producing bacterium of sufficient activity to change the local acidity of the saliva at the point in question well below the iso-electric point of that saliva. The organisms which do this must have a supply of starch or carbohydrate from which they produce the lactic acid for still further reducing the hydrogen-ion concentration.

In a normal condition of the mouth the factor of safety is sufficiently on the alkaline side of the iso-electric point of saliva to maintain a constant potential between the ionic calcium of the saliva and of the tooth to keep calcium continually entering the tooth structure. Under certain conditions, such as fever, pregnancy, etc., this normal environment of the mouth is changed. Since every substance, when placed in a liquid medium, tends to produce ions of its structure in that medium, there is always maintained a balance between the forces, expressed as valency between ions, and the forces of solution and crystallization. In pregnancy this normal balance is broken through a change of environmental fluids, blood, and saliva; calcium goes out of the tooth under this law of ionization. Slowly but definitely the teeth lose some of their substance as ionic calcium compounds. The factor of safety being reduced, it is much more easy for local zones of bacterial growth to create a condition just over the iso-electric border on the side of relative acidity, with the effect that in such teeth, and with such an environment of saliva, the decay takes place very much more rapidly than in an ordinary mouth where the normal factor of safety is in general maintained. We must remember that acidity and alkalinity are relative factors dependent upon the iso-electric point of that individual's saliva. In case, then, the individual has a high ionic calcium of the blood, he has a high capacity for maintaining the alkalinity of the saliva; and this type of individual tends, as we have shown, to tear down alveolar bone about the tooth to maintain an extreme alkalinity, but in so doing produces an environment which accomplishes two things. It prevents dental caries by its large alkaline factor of safety and it tends to make the enamel of the tooth more dense than normal. This type of individual tends to have the glassy dentin on all surfaces of abrasion.

Our studies have shown, as have also the studies of others, that practically all teeth before eruption are in a condition in which the enamel will stain very perceptibly with silver nitrate and other stains, for an appreciable distance into the enamel, and that after eruption the enamel surfaces of the tooth undergo a change in which there is apparent increase in the density of the surface enamel so that they stain much less readily, and in old age and in all adult life free from caries, the surface layer of enamel is but slightly penetrable by silver nitrate. This process of hypercalcification (as I have chosen to term it) is pretty largely completed by the twentieth year of life, after which, except in periods of disturbed saliva, there is little tendency to dental caries.

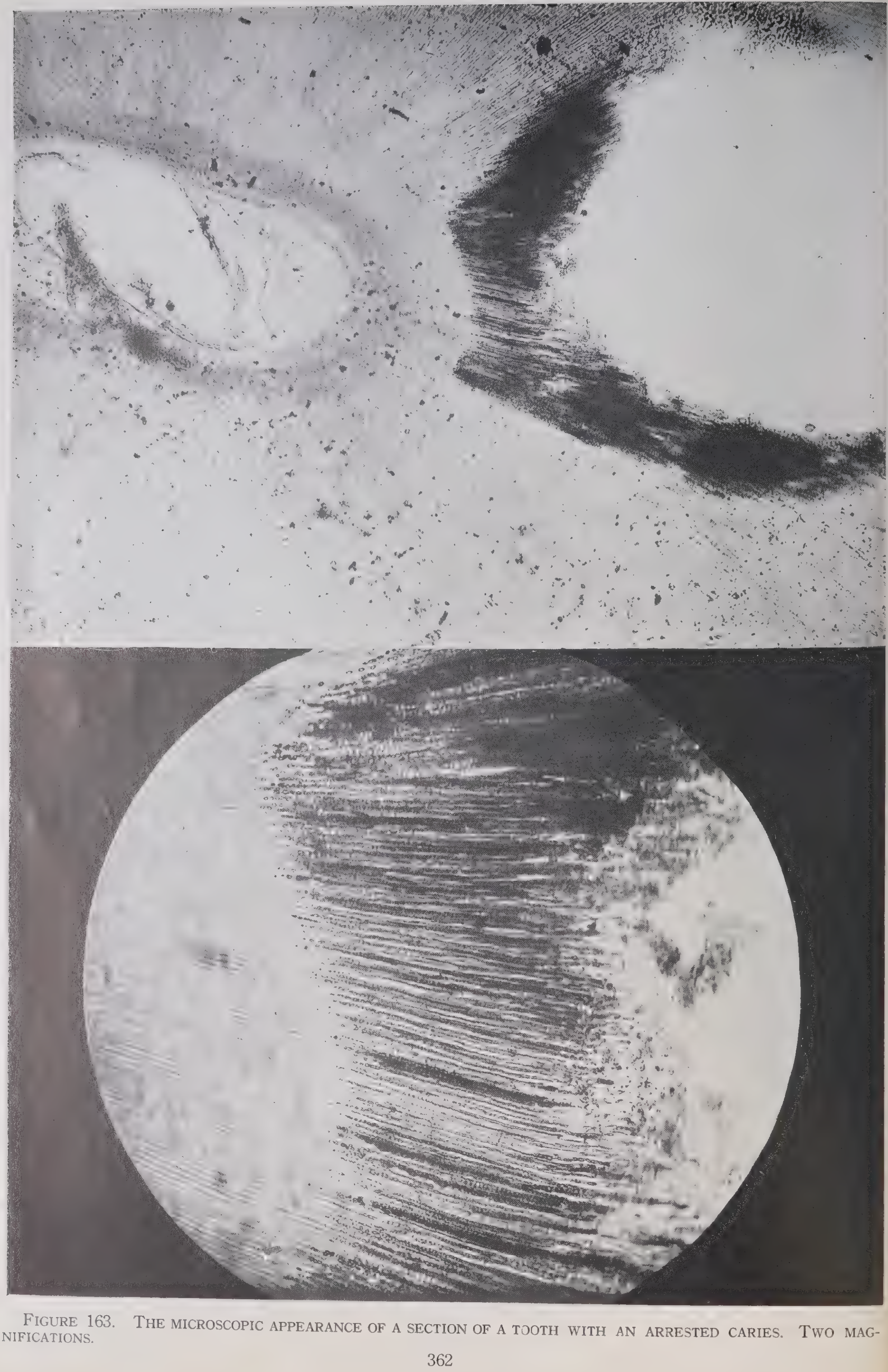

FIGURE 163. THE MICROSCOPIC APPEARANCE OF A SECTION OF A TOOTH WITH AN ARRESTED CARIES. TWO MAGNIFICATIONS.

We have, therefore, in the change of environment, as provided by the change in the hydrogen-ion concentration of the saliva, its iso-electric point, and its ionic calcium, factors which enter largely into the condition of immunity and susceptibility to dental caries. It is a quite frequently seen phenomenon that a mouth, in which caries has been active, has suddenly, ceased to be so, and *vice versa*. Among the factors which enter into life to bring about these changing states, are febrile disturbances, physical and nervous overload, and pregnancy. An illustration of the effect of the latter upon a tooth, is shown in Figure 163, which shows a cross section of the tooth with a deep caries extending nearly to the pulp. It will be noted that a secondary dentin has been thrown down on the pulpal surface beneath the approaching caries; and this caries, which at one time was active and progressive, ceased to be so, and there is a strong demarcation in cross section between the zone of living dentin and the dead dentin of the caries. The period at which this happened, as determined by the patient's report of the condition of the tooth, corresponded with the period of pregnancy and lactation, and this was an individual with normally a high defense. In the higher magnification shown, the etching out of the dentinal tubuli is very clearly disclosed; and it is both interesting and significant that, in this case, the zone of limitation of the advancement of the bacteria into the dentinal tubuli is distinctly marked. The irritation of the toxic bacterial products undoubtedly sufficed to produce the reaction within the pulp, which caused the laying down of the secondary dentin.

SUMMARY AND CONCLUSIONS.

Dental caries is dependent upon the following factors:

(a) **A reduction in the hydrogen-ion concentration of the normal environment of the tooth.**

(b) **An acid producing bacterium.**

(c) **A change in the chemical constituents of the pabulum bathing the tooth.**

CHAPTER XXX.

THE NATURE OF SENSITIZATION REACTIONS.

PROBLEM: Do dental infections produce sensitizations of an anaphylactic character?

EXPERIMENTAL AND DISCUSSION.

For several years, I have been seeing illustrations of systemic diseases, the chief characteristics of which were quite unlike those of ordinary bacterial invasion, and which seemed very definitely to be related to dental conditions. The following is the history of such a case previously reported by me.

The patient, a man about forty, presented with the following history. For two years he had been affected with recurring headaches followed by digestive tract disturbance (not preceded by it) and accompanied by lassitude; which made it practically impossible for him to carry on his business. For the last six months prior to his coming, he had been practically compelled to abandon his business, and was in a state of mental discouragement and depression as a result of his physical disability. An examination of his mouth showed very extensive periodontoclasia, and, bacteriologically, very profuse fusiform and spirochete infection. At our first sitting we curetted one-fourth of the mouth. Within a few hours he suffered a violent attack of his characteristic headaches, followed before morning by acute digestive tract disturbances, with purging, cramping, and mucous stools. This attack lasted for a couple of days. After it subsided, he reported that he felt better than he had for some time, and was convinced that the reaction was related to his dental condition and its treatment. In about five days the other half of the upper arch was curetted, which operation was followed by a similar reaction though less severe. Similarly, at intervals of about five days, the lower arch was curetted, one-half at a time, during which time he was continually improving. Soon after the gingival infection was obliterated, a couple of teeth, being considered too far advanced for treatment, were extracted. His health returned to normal and has remained so for ten years, except that on many occasions he has felt the beginning of the old symptoms returning, has presented promptly for treatment, and generally in proportion to his development toward the condition of sensitization, he responded in the same manner to treatment, though with much less severe reaction. He became so familiar with his symptoms that on several occasions he telephoned during the day saying, "I feel one of my old attacks coming on. How quickly may I have a treatment?" which would always be given at the earliest possible moment, sometimes within an hour or two. The treatment was successful in aborting the attack in proportion to the earliness in the attack when the treatment was instituted. Many forms of treatment were tested, such as the injections of emetin and succinimid of mercury, subcutaneously, which had but slight effect. We will refer to the nature of these symptoms in later paragraphs.

Another case with a similar sensitization complained because we did not do more of the curettage in gingival treatment at the first sitting; and when we advised her that she probably would have a reaction and to let us know regarding it by telephone the next day, she assured us that she would either telephone or come in. On the next day, she found herself feeling so miserable that she not only did not come to the office but did not even get up from her bed, even though the telephone was on a stand near the head of her bed. She said, "Well, what's the use of telephoning? He knew I would be sick anyway." She really did not have energy enough to reach the telephone, and report. Similarly, after her first acute reaction was over, she felt distinctly better. We have also reported previously, in the paper referred to, the cyclic nature of these sensitizations, some having a period of five or six weeks in the early stages, or even several months, with the periodicity shortening to two or three weeks, and finally even less.

Occasionally, though not generally, we found that after the extraction of infected teeth without gingival infections, the patients had very marked reactions which were more like toxic processes than bacterial invasions. A careful study of a large number of these cases suggested that this toxic factor was in many instances very important, and seemingly more important than the bacterial invasion factor. We, accordingly, instituted a long series of experiments to determine the nature and qualities of the toxic substances in teeth, if such existed, and their effects on animals both directly and in connection with the bacterial strain

SENSITIZATION REACTIONS TO TOOTH TOXINS

Group	No. in Group	Days Lived	Loss		
			Actual	%	% per day
Organisms washed and suspended in NaCl	8	7	203	18	2.6
Whole Culture Group I	16	6	209	18	3.0
Whole Culture Group II	55	7	226	20	2.9
Filtered Tooth Washings	13	5	191	19	3.8
Unfiltered Tooth Washings	8	12	221	22	1.8
Sensitized Rabbits	4	**4**	94	10	2.5

FIGURE 164.

found in these teeth. Figure 164 shows the results of these studies. It will be noted that in the group of animals inoculated with the washed organisms suspended in sodium chloride, the loss in weight per day was 2.6; and in the unwashed or whole culture, 3.0, the dosage being adjusted to approximately the same number of organisms: namely, the amount that would be in 1 cc. of a 24 hour culture broth. A second and larger group of 55 rabbits receiving the whole culture, had a loss of 2.9. The average length of time, however, that the animals lived in these three groups was approximately the same: namely, 7 in the first, 6 in the second, and 7 in the third. When, however, animals were inoculated with filtered tooth washings, the average length of life was 5 days for 13 rabbits, with a loss per day of 3.8 per cent; and with the unfiltered washings, they died on an average of 12 days, with an average loss per day of 1.8 per cent. In another chapter I have discussed the probable reason for the greater toxicity of the filtered washing than the unfiltered, as judged from the length of time the animals lived. When, now, we compare with these figures the effect of injection of the whole culture into rabbits that had been previously sensitized by injecting, intravenously, a small quantity of the filtered washings, (not the total quanity, as above, from the tooth in question and from the chips of which the organisms were grown for this whole culture), this remarkable result came out, that the average length of life of 4 rabbits so treated, was 4 days after the injection of this culture (Note that this is less than the average length of life of rabbits in any of the preceding groups) and the percentage loss per day, per rabbit, was 2.5. Two possible factors, at least, were possibly contributing, one a sensitization and the other an additive injury. The fact, however, that some rabbits not included in this group, died within a few minutes or hours after being injected with the culture where they had previously been sensitized by the use of the toxic substance from that tooth, precludes, in those cases, the possibility of the explanation's being due to an additive factor, since they died from typical sensitization phenomena, such as scratching the nose, violent peristalsis of the intestines, labored breathing, etc. Another argument against this being an additive factor is the fact, that when succeeding injections below the lethal dose of a given culture are used in the same animal, it tends to build up defense, which, with most cultures, can be brought to a state of very high toleration, permitting of massive doses without lethal effects.

In the preceding chapters, 17 and 20, I have discussed the capacity of teeth for containing toxic and bacterial products, and have demonstrated that the quantity therein may be ample to produce very profound disturbances, both in animals and in humans. I have brought out the fact that approximately five per cent of even a well root-filled tooth is fluid, which may be culture media or toxic product; and also that when animals were inoculated with the bacteria-free soluble toxin derived from the infected tooth, they developed very definite and characteristic symptoms, and also that, in some instances, they were much more sensitive and susceptible to the organisms cultured from that tooth; that the toxic substance taken from teeth tended to disturb metabolism and start a procession of changes which usually terminated in death, and usually with marked changes in the digestive tract, with great loss of weight. In another chapter, we will study the structural changes of tissues as a result of these processes. It is, however, important to note here that, in some instances, an acute diarrhea was produced in from thirty minutes to two hours after the injection of this toxic substance, and animals not infrequently died having had blood-streaked mucous stools. It is, therefore, apparent that we are dealing with substances of profound toxicity. There are, however, many types of sensitization which differ from these expressions of toxicity. In one case, we are dealing with systemic poisoning from a violently acting toxin; in the other, with a state of exalted irritability of tissue, a true anaphylaxis or allergy. While this is not intended to be a treatise on immunology, it seems necessary for me to give a brief review of the conditions which obtain in true anaphylaxis.

When proteins are injected parenterally into suitable animals, they may pass through the blood stream without any apparent effect. If, however, at a subsequent date, particularly from six to twenty-eight days after this first injection of protein, which may have been a very small dose, there is again injected into the circulation of that animal some of the same protein, it will produce an entirely different effect. In many instances there will be disturbed breathing, itching of the skin, itching of the nose, and if the animal is particularly sensitive it may die in a few minutes from spasms of the bronchioles, with continuation of cardiac function after the cessation of respiration, or the animal may entirely recover. The processes that have developed are somewhat as follows:

The first or sensitizing dose sets up in that animal the development of an active mechanism capable of splitting that protein, in order that it may be eliminated from the blood. The first or sensitizing dose may have floated in the blood stream largely for days before that mechanism had been sufficiently perfected to split it. With the consummation of that mechanism the animal was able to split large quantities of this protein in a short time; but since, according to Vaughn, all proteins split into a poisonous and nonpoisonous part, the poisonous part being the same in all proteins, there is set free in the system a quantity of poison which, if not immediately eliminated, does harm by its presence. This constitutes the sense of illness from disease and the cause of pyrexia. Vaughn states that the amount of poison in a gram of cheese, when thus split, is sufficient to kill seven hundred guinea-pigs. The first or sensitizing dose may in some instances be only a minute fraction of a gram and yet be sufficient to prepare the body to react vigorously against a second dose. The introduced protein is spoken of as the antigen and the substance which the body develops as the antibody. An illustration of the extreme delicacy of this mechanism is familiar to all in hay fever. The individual who suffers from hay fever is usually sensitized to the pollen of some weed, grain, or flower, and the amount that is necessary to bring on a reaction is so infinitely small, that it may drift invisibly in the air and doubtless can be less than a millionth part of a gram. In Part Two, under Other Tissues, we give illustrations of anaphylaxis to dental infections in addition to those given here.

With these fundamentals of protein sensitization in mind, let us review the following case from practice: The patient presents with a history as follows: For some time he had been suffering

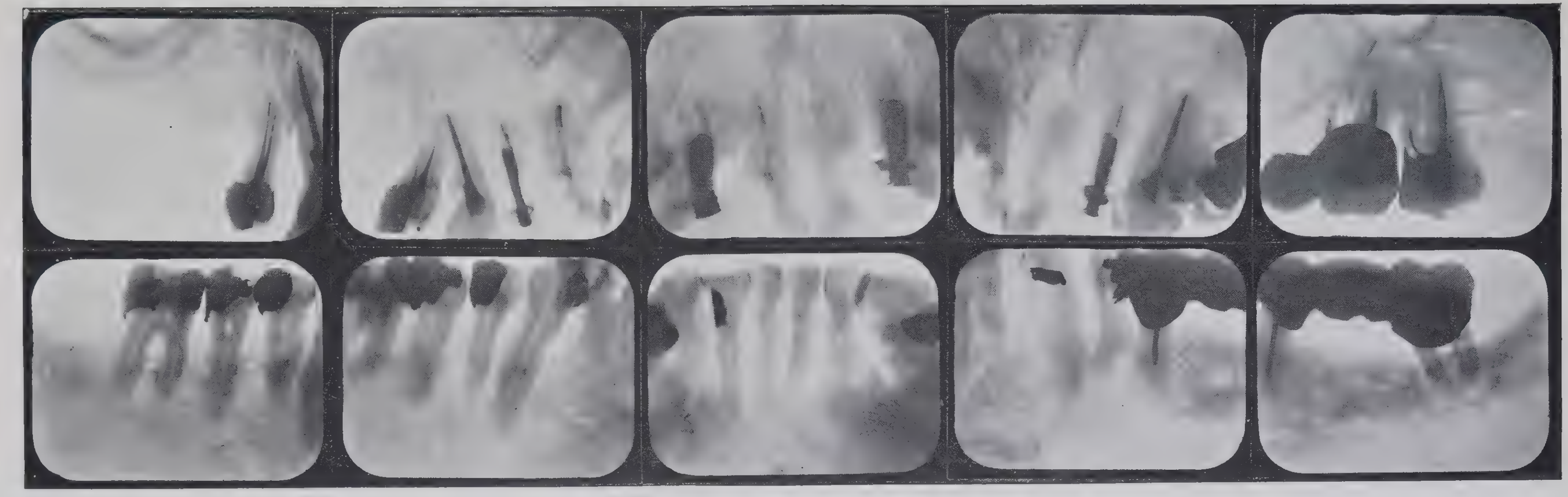

Figure 165. Roentgenographic appearance of the teeth. Patient suffering sensitization reaction from his dental infection, shown in Figure 166.

from recurring attacks which were increasing in severity and frequency, closely resembling hay fever but not related to any season or locality. Careful and exhaustive studies had been made by specialists in different cities to find the nature and cause of his sensitization, without avail. Figure 165 shows roentgenograms of his teeth which have evidently been infected for years, but have given him very little inconvenience or disturbance. Upon the extraction of the first tooth, he developed, within six hours, the most severe attack of his sensitization reaction he had ever had. Figure 166 shows his appearance which lasted for days. His eyes were bloodshot; tears would drip from his eyes; and the mucous would almost stream from his nostrils. His headache was extreme. The inflammation involved all mucous membranes of the mouth, nose, eyes, and throat, and extended around his eyes, nose, and mouth, approximately half an inch. The night of his first attack he did not sleep a moment, according to his report, and his distress was pathetic. The use of mild sprays, carrying adrenalin and cocain, greatly relieved his suffering. The tooth that was extracted was cultured, and the toxin washed from it injected into two rabbits. Both developed extreme inflammations. In one the eyes were bloodshot and tears running in forty minutes; and for two days profuse discharge was coming from its nostrils, shown in Figure 166. Note: This animal is not reacting from anaphylaxis, not having been previously sensitized. It is apparent that we are dealing here with a substance which has profound tissue affinity, and which is not bacterial, though it may be a bacterial product, since the fluid injected into the rabbits had been passed through a Berkefeld filter and was bacteria-free. Subsequently, the balance of the infected teeth were removed, a few at a time, without serious reaction, and the patient's health very rapidly and splendidly improved, and for a year he has been without a single recurrence of his old and troublesome affection. Since the reaction in the rabbits was produced by the filtered washings of the tooth, we cannot interpret their disturbances as a tissue affinity quality of a particular bacterium injected.

A striking illustration of an anaphylactic state or sensitization produced in a rabbit is as follows: Rabbit 184 was inoculated on Feburuary 18th with a salt solution washing of two crushed teeth, (biscuspids,) intravenously. Its weight at this time was 855 grams. On the 23rd its weight had increased to 920 grams, and on March 1st to 1046 grams. On March 2 it was inoculated

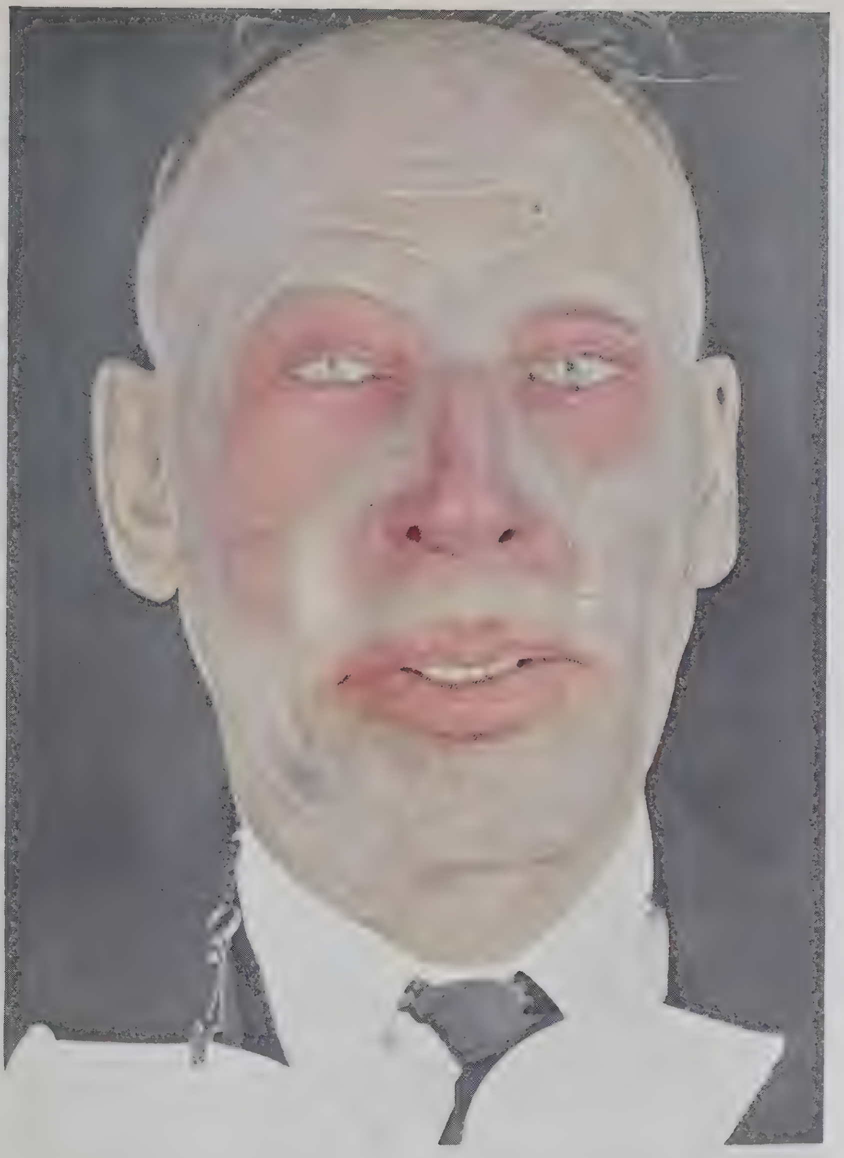

Figure 166. A, a recurring acute inflammatory sensitization reaction produced in a patient by his dental infection; B, a rabbit which developed acute lacrimation and rhinitis in forty minutes after inoculation with washings from this patient's crushed teeth.

with the culture grown from these same teeth; weight 1075 grams. Within three hours after the inoculation of approximately 1 cc. of the whole culture, which is the bacterial suspension in the media in which they were grown, the rabbit died. The postmortem examination showed the liver to be slightly enlarged, stomach normal but very pale in color, lymph glands surrounding the stomach markedly enlarged, edematous, and resembling grapes, spleen enlarged, and lungs collapsed. The diagnosis of cause of death was anaphylaxis.

The literature and teaching of the past have placed a particular emphasis on certain groups of symptoms as being characteristic of sensitization, expressing themselves chiefly in the skin, air passages, and bronchioles. We have, accordingly, been in the habit of looking for symptoms as the chief ones expressive of anaphylactic reactions. We are, however, coming to believe that many tissues respond with true anaphylactic reaction which we have not regarded as likely seats of this allergy.

Inasmuch as individuals sensitized to foreign proteins have certain definite reactions to that foreign protein, we have made animal studies to determine whether the introduction of the toxic substances taken from the teeth would develop in animals a state of anaphylaxis which could be demonstrated by dermal and other reactions. We have found that the toxic substance taken from some teeth, when injected into rabbits, does produce in from six to twenty-eight days a true state of anaphylaxis, as evidenced by the fact that they showed definite dermal reaction to either the placing of the toxin on a scarification or the injection of a minute quantity of it in the superficial layers of the skin. We have found also that in some cases this toxic substance sensitizes the animal not only to this toxic substance which, though bacteria-free when injected, prepares that animal to respond to a washed suspension of the organisms grown from the tooth which produced that toxin, but also to the culture medium in which those organisms have grown. A rabbit inoculated with a bacterial suspension grown from the tooth from which the toxin was extracted to sensitize that rabbit, when the suspension was inoculated into this rabbit, died within two minutes showing the classical symptoms of shock, or true anaphylaxis. Studies of this problem on several hundred rabbits reveal that all infected teeth do not have this toxic substance in the same quantity nor do they have the same qualities. Those familiar with the problem of sensitization reactions in animals understand that the rabbit is not a favorable animal to use for this investigation, in that it is not highly sensitive to anaphylactic reactions as compared with the guinea-pig. We have used both guinea-pigs and rabbits. Particularly because of our other observations with which we wanted to make comparisons, such as elective localization of the organisms involved, we decided to use the same type of animals for our sensitization tests. We have deemed that there would be some advantage in not using animals that are too sensitive to anaphylactic reaction.

The recent literature has stressed the relationships between anaphylaxis and shock, and these in turn with reaction effects of animals inoculated with histamine. With this latter the animal dies from failure of respiration, usually in a few minutes after injection, during which time it exhibits a group of symptoms very similar to those exhibited by animals dying from anaphylaxis from the injection of a protein to which they have been previously sensitized. All such animals exhibit characteristic disturbances of the lungs and viscera, as marked engorgement of the capillaries and mesentery and visceral arterioles.

Figure 167 shows the normal vascularization of the mesenteries and intestines of a rabbit. Note the blanched white condition of the mesentery and the constricted blood vessels of the intestine. The specimens shown in Figure 168 are from a rabbit dying from a sensitization produced by crushing the tooth, injecting this into a rabbit, and later the rabbit was inoculated with the culture grown from this same tooth. This rabbit died in two minutes with the characteristic reactions exhibited in anaphylaxis. In the inoculation of over fifteen hundred rabbits for various purposes, no rabbits have died quickly, following inoculation as this rabbit has done, except where previously sensitized by such a process as this inoculation with the washings of a crushed tooth. Note the engorgement of the blood vessels of the intestines and mesenteries. Figure 169 shows the same condition in the similar tissues of a rabbit inoculated with histamine.

This condition is not comparable to the reaction produced in the rabbit injected with the material taken from the tooth of the patient referred to above shown in Figure 166, which symptoms developed about forty minutes after the first injection, since that rabbit was not sensitized by a previous injection. This reaction was probably a tissue irritation and in addition an elective localization. In other words, the rabbit shown in Figure 166 is not an illustration of allergy or anaphylaxis.

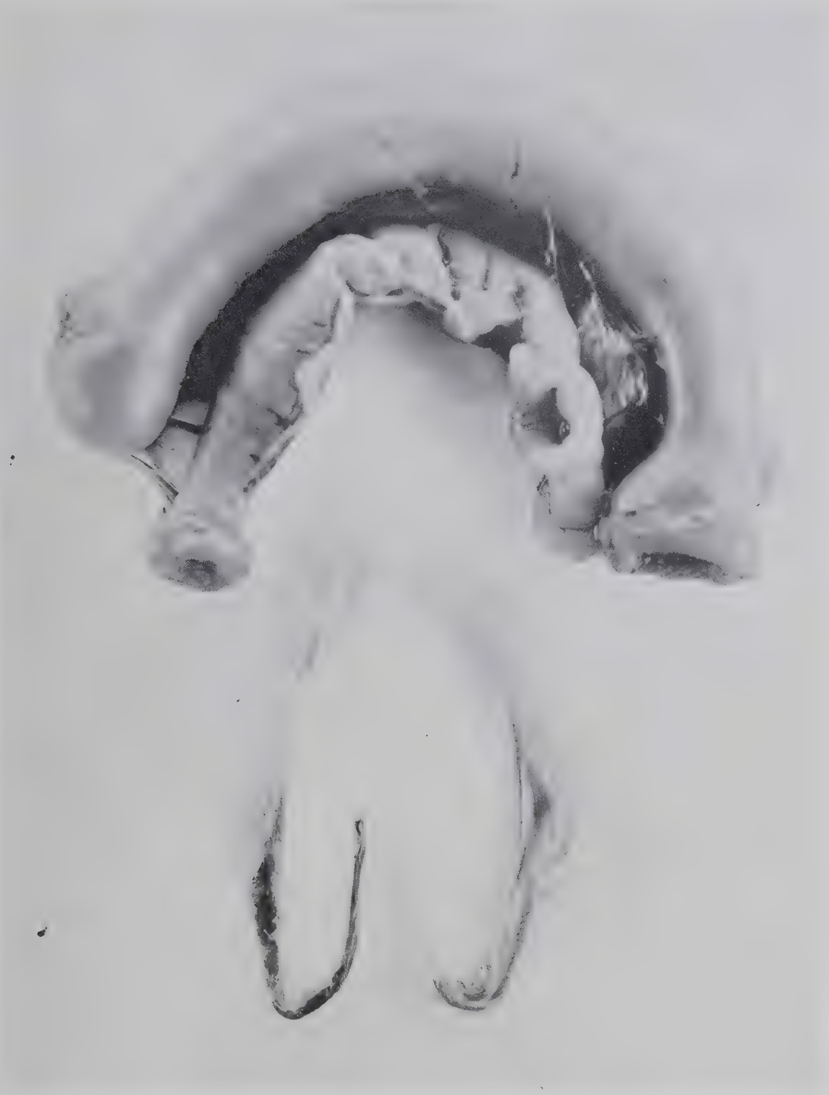

FIGURE 167. NORMAL VASCULARIZATION OF MESENTERIES, INTESTINES, AND TESTICLES OF A RABBIT.

In studying the skin reactions of animals, we have found two distinct types: First, appearing in from a half minute to thirty minutes and subsiding in a few hours, characterized by a central wheal from a fourth of an inch to one inch in diameter, which is raised, edematous, and hard, and surrounded by an erythematous area from a half inch to an inch and a half in diameter, as shown in Figure 170. We have also found a secondary reaction developing in from six to eighteen hours, which may last for a few hours or

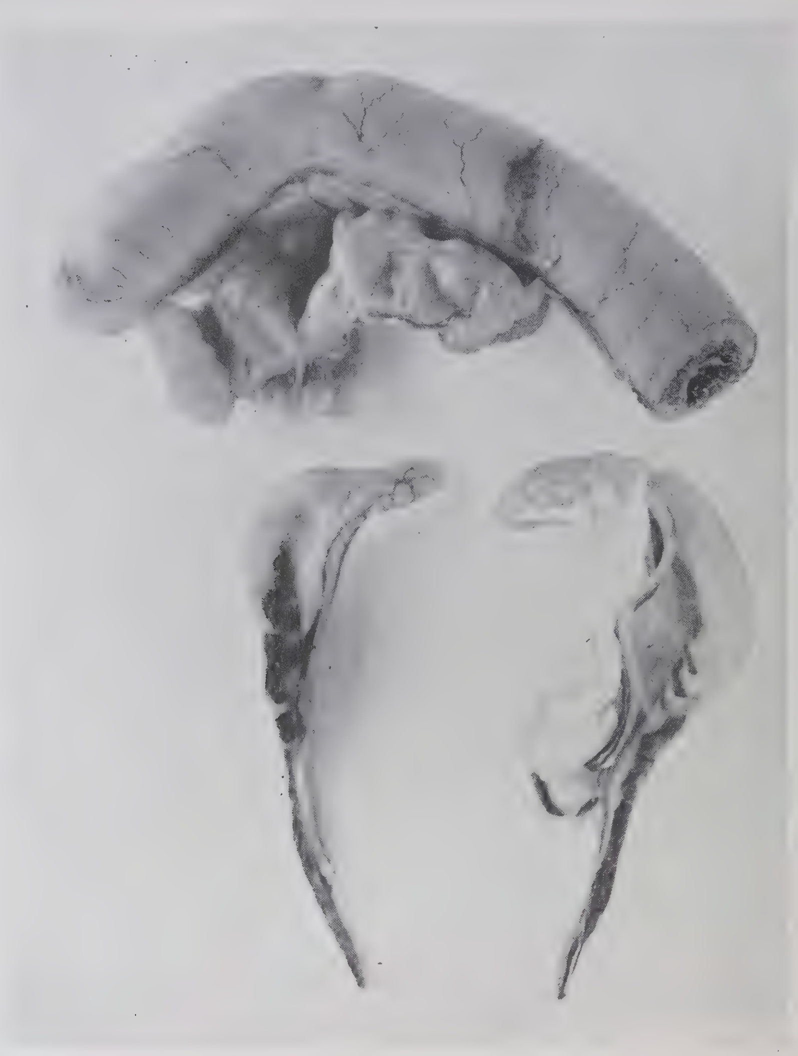

FIGURE 168. THE VASCULARIZATION OF MESENTERIES, INTESTINES, AND TESTICLES OF A RABBIT SENSITIZED WITH THE WASHINGS OF A CRUSHED TOOTH.

for several days, and in which the area originally occupied as the central whitish wheal is now deep pink and surrounded by a more or less deep pink area, often with an increase of temperature of the surface and the appearance of a scald or burn that is just short of the production of the water-blister. These vary in intensity. These are the characteristic reactions that make up the Schick test for the identification of diphtheria, as expressed in the first reaction, and the tuberculin test for tuberculosis as expressed in the second reaction.

Having demonstrated the presence of this condition and reaction in animals, we have made tests upon many patients to

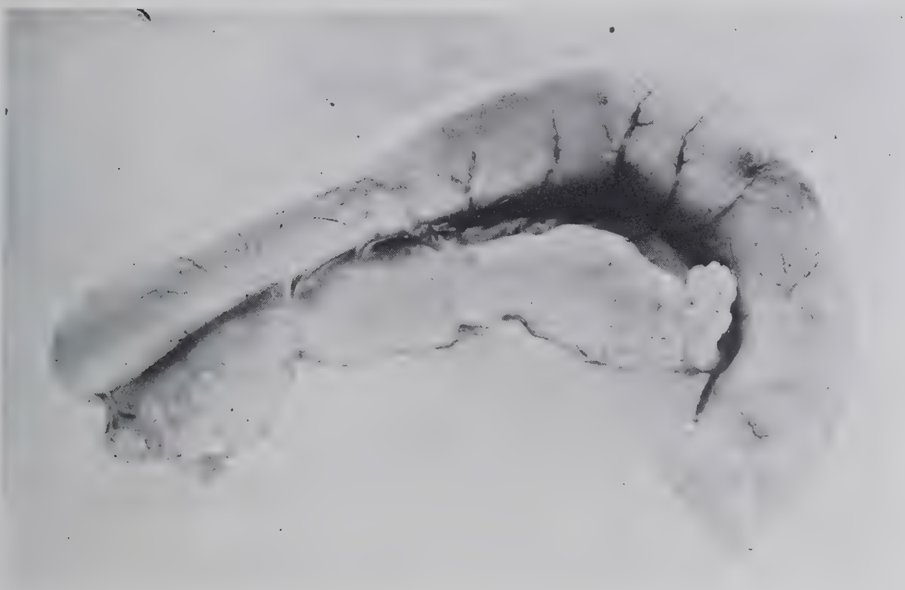

FIGURE 169. THE VASCULARIZATION OF THE MESENTERIES AND INTESTINES OF A RABBIT INJECTED WITH HISTAMINE.

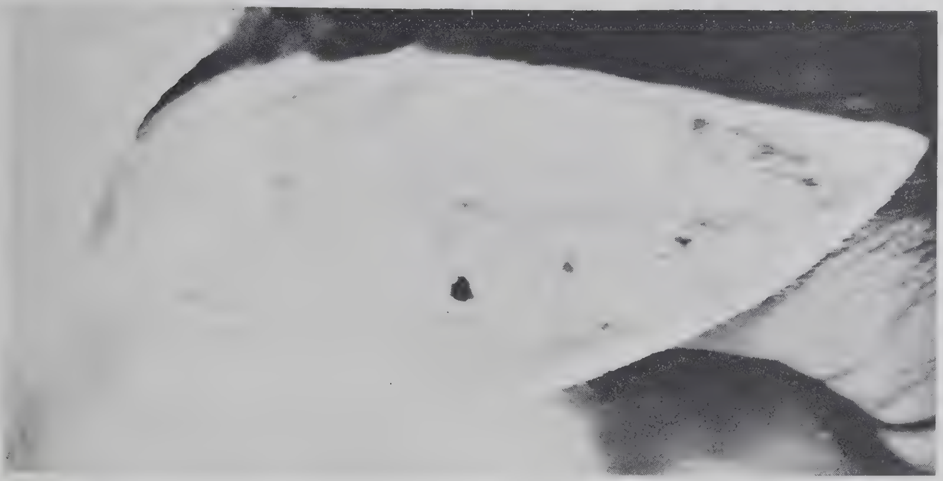

FIGURE 170. TWO MILD AND ONE STRONG POSITIVE REACTIONS IN A RABBIT'S EAR THAT HAD BEEN SENSITIZED TO A DENTAL TOXIN.

determine whether or not they would develop either or both of these reactions. Figure 171 shows the primary reactions of the patient shown in Figure 166, when tested with the extract of the toxin from his tooth, prepared by three different methods. Figure 171-B shows this same arm with its secondary reactions. The essential features about this patient's case are that he had recurring attacks, cyclic in nature, the periods of which had been shortening for years and which latterly had become weekly or biweekly. This readily eliminated the possibility of its being seasonal and related to pollens, etc. If it be a true allergy, the dermal test should give the typical Schick reaction, provided that it is possible to extract the toxic substance which is producing the antigen, or which is acting as the antigen. Many methods have been used for extracting the sensitizing substance, including those generally in use for selecting the antigen from pollens, foods, etc. We have here evidence both that the patient is suffering from a true allergy, the antigen of which is coming from his infected teeth; and the antibody-antigen reaction takes place in the mucous membranes of the eyes, nose, and mouth. The fact that he had no recurrence for a year afterward, except a slight suggestion of an irritation at the time of the hay fever of August, is a strong indication that his primary disturbance was of this origin. It will also be noted that this patient had a strong secondary reaction from this original test and which reaction none of the controls of the six members of the staff developed, an additional evidence that we are in this case dealing with a specific reaction to a specific antigen.

In many of these cases we have found the patients sensitized to the toxic substance as extracted from infected teeth of other individuals, and in other instances, evidences of a marked specificity to the infection of their own teeth. In cases where the toxin was extracted from the patient's own tooth, the test, when positive, developed more rapidly and usually more severely. We have also found a difference in the reaction effect from toxin taken from teeth of periodontoclasia conditions from those with chronic periapical involvements. The data are not sufficient for making deductions or generalizations.

In addition to the regular or classical symptoms we are now coming to recognize other lesions as being directly related as true allergies. Conspicuous among these are skin disturbances, expressing themselves as dermatoses which may be very persistent and painful. Such a one is shown in Case No. 1334, a professional pianist who became incapacitated by the presence on the palmar surfaces of his hands of a scaly dermatosis accompanied by marked stiffness of his fingers. His hands would crack to or near the point of bleeding. (See Figure 172-A before treatment; and,

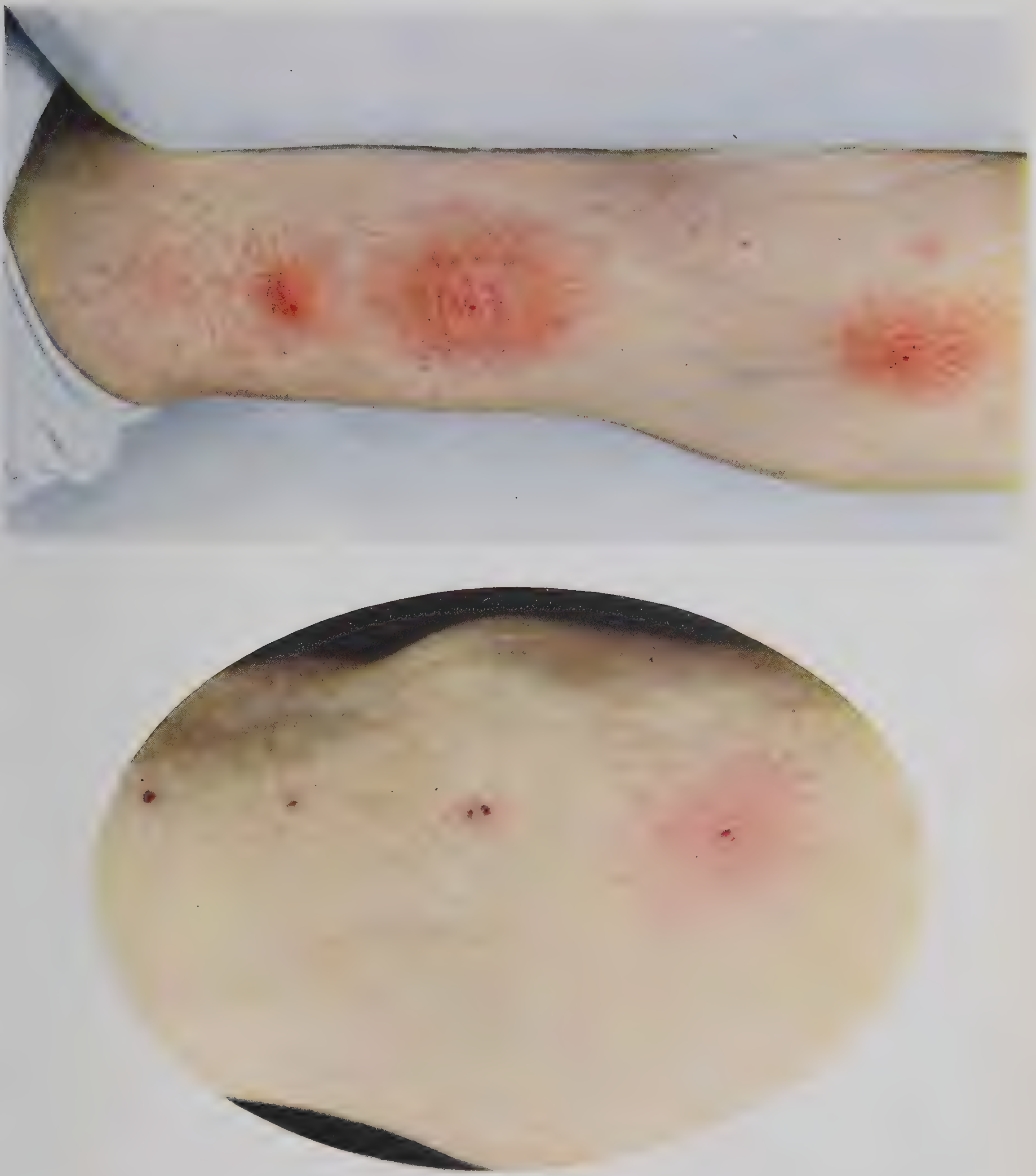

Figure 171. Upper. Three positive primary dermal reactions on the arm of the patient shown in Figure 166. Lower. One positive secondary reaction from same patient.

[chap. xxx—the nature of sensitization reactions.]

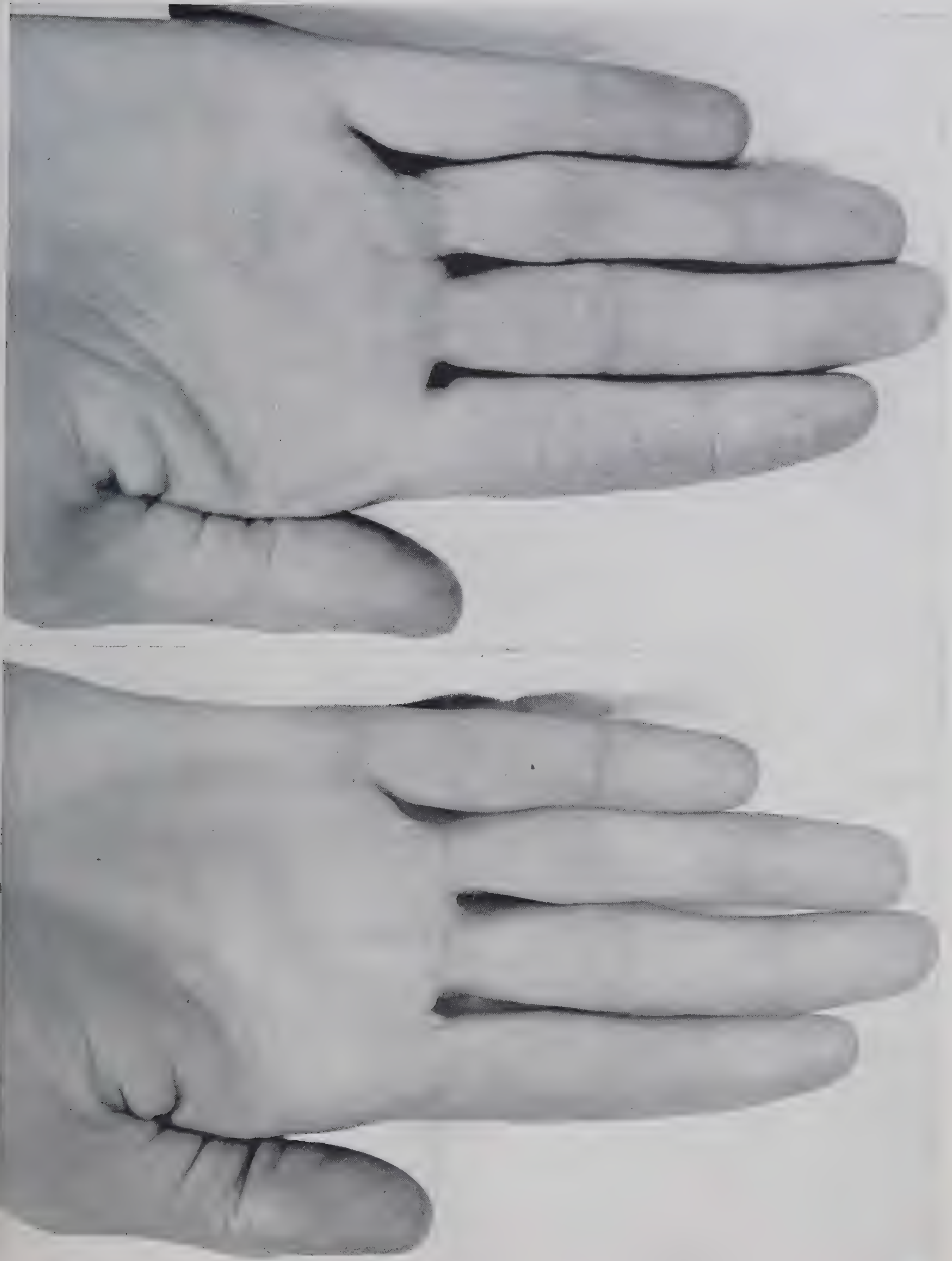

FIGURE 172. A SCALY DERMATOSIS, WITH MARKED STIFFNESS OF FINGERS. A, UPPER, BEFORE REMOVAL OF DENTAL INFECTION; B, LOWER, AFTER.

172-B, after treatment.) The condition did not respond to medication. The extraction of an infected tooth, shown in Figure 173, completely eliminated his trouble, and at the same time a condition of lassitude and mental languor. An extract of the toxic substance taken from his tooth was applied as a dermal test and in thirty minutes produced the enormous wheal shown in Figure 174. The secondary reaction in this case was negative, as shown in Figure B of the same figure.

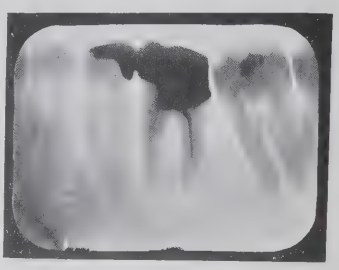

FIGURE 173. THE DENTAL INFECTION INVOLVED IN THE SKIN LESION OF FIGURE 172.

These studies have suggested that the toxic substance which is present in the patient's body, might possibly be found in the patient's blood, if a test could be developed which would be sensitive enough to record it, since, apparently, infinitely small quantities are adequate to produce very marked tissue reactions in sensitized tissues.

Another type of skin reaction, typical of this group, showing dermal sensitization is shown in Figure 175. A shows a lesion on the patient's elbow which was distinctly defined, slightly raised, brownish in color, without erythema, with a tendency to scaling on the affected surface. B shows two positive primary dermal reactions to a toxin extracted from his tooth. The secondary reaction in this case was negative. After the removal of his dental infections and before they were completely removed, his skin disturbance entirely disappeared as shown in C. My interpretation both of these primary and secondary reactions is given in Chapters 45 to 56 on Interpretation.

Figure 176 shows the roentgenographic record of some of the teeth of this patient. It will be noted that there are very extensive areas of bone absorption, both at the gingival borders and at the root apices. The local dental pathology corresponds with his clinical history. He is a man of unusually high defense, and has carried this large amount of gingival and apical infection for a

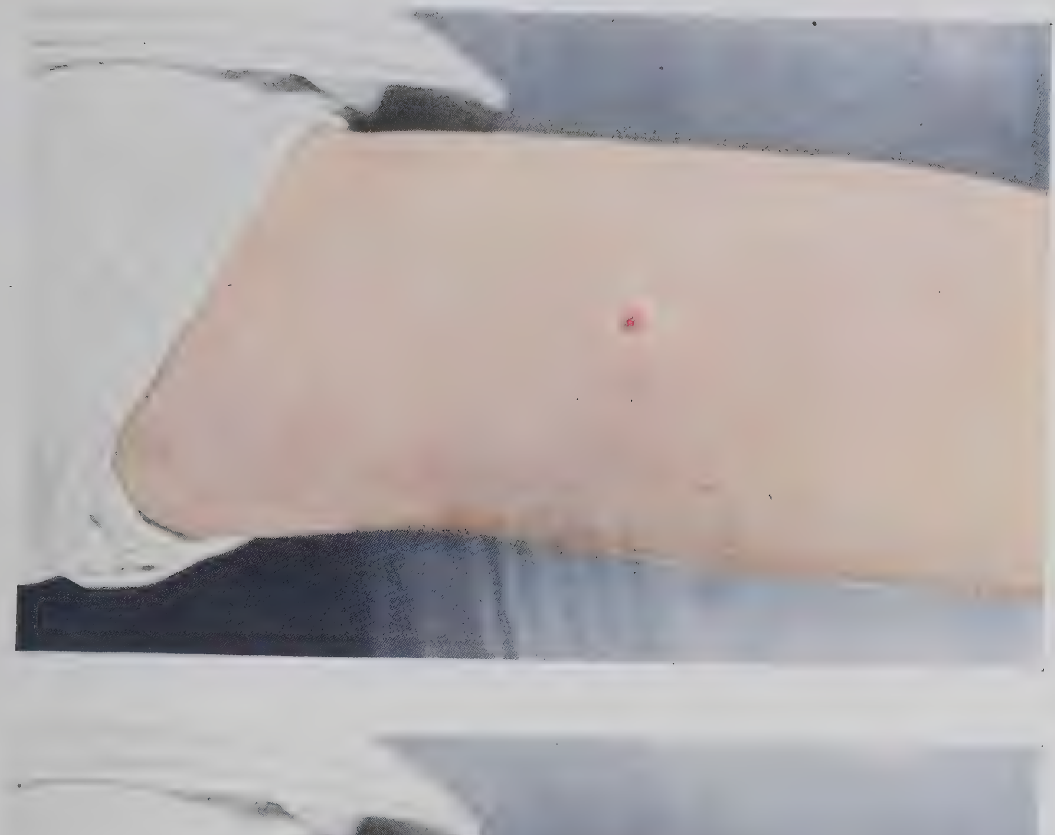

FIGURE 174. THE DERMAL REACTIONS OF THE PATIENT IN FIGURES 172 AND 173. LOWER, POSITIVE PRIMARY; UPPER, NEGATIVE SECONDARY.

[CHAP. XXX—THE NATURE OF SENSITIZATION REACTIONS.]

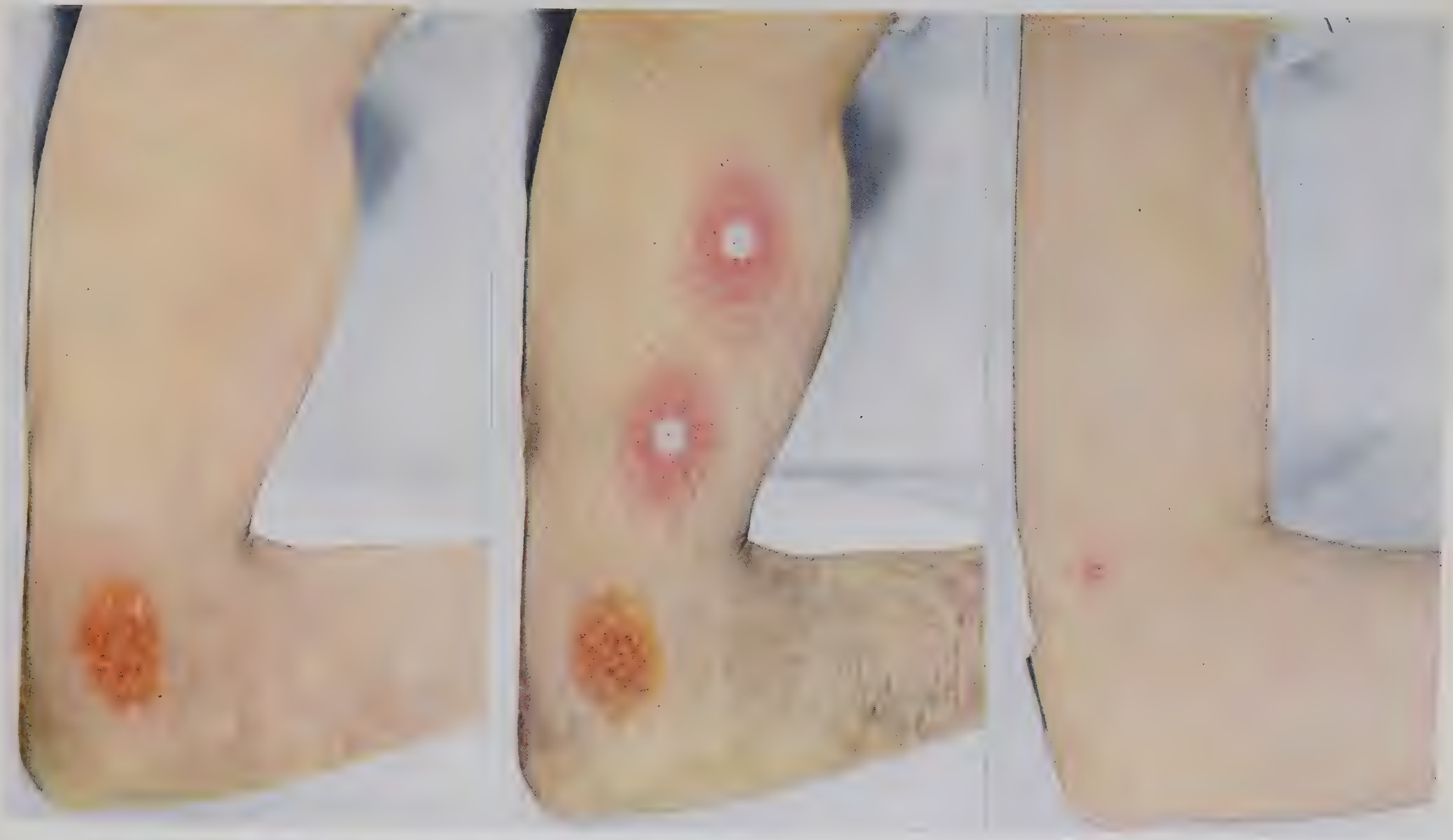

Figure 175. First, a persistent dermal irritation; second, the same arm with two primary positive reactions from his dental infection; third, the same arm one week later. There was no recurrence in nine months.

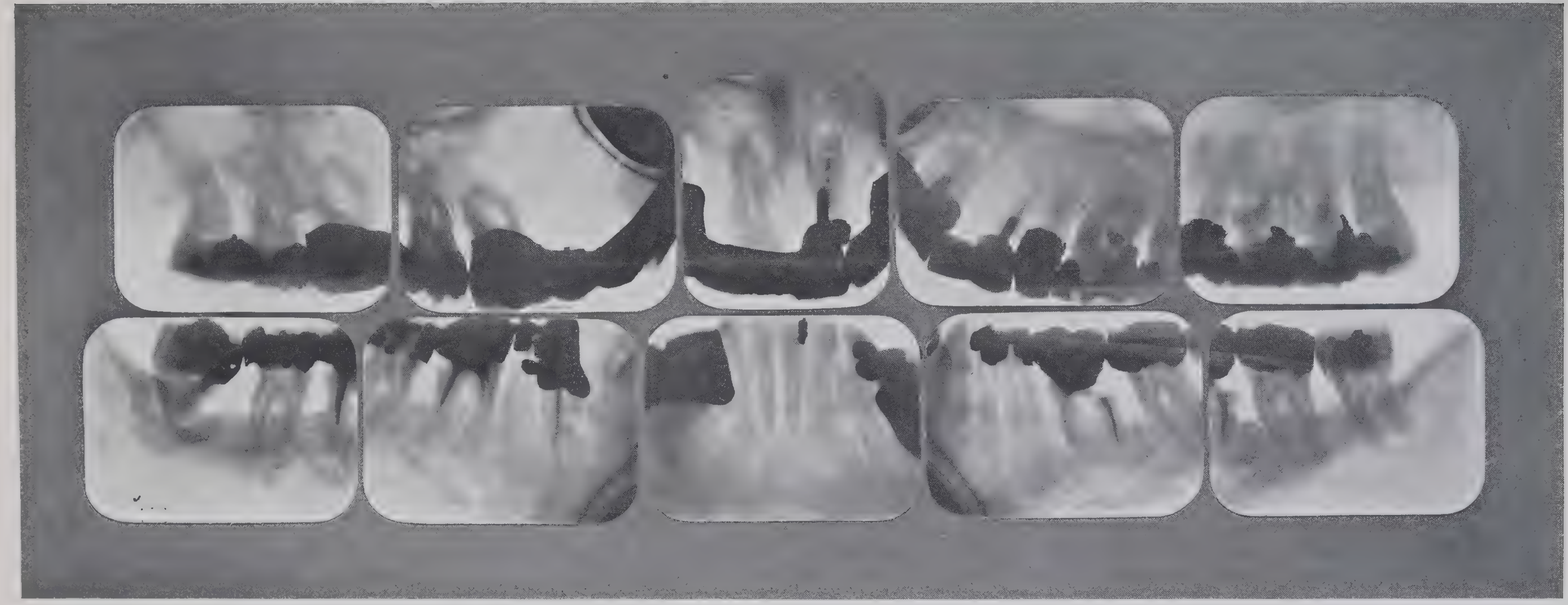

Figure 176. Roentgenographic record of the teeth of the patient shown in Figure 175.

number of years. A constant passage into his system of the irritant protein compounds from these teeth, seems to have created a state of hypersusceptibility and reactivity.

At this point I wish to discuss an important phase of the cases which, so far as we know, is entirely new. When we compare the type of systemic disturbance with the researches on the variations in chemical constituents of the blood, this important new fact has come out. In a group of individuals suffering from typical sensitization reactions, we found that the type of dental pathology, as expressed in the mouth, is that of extensive or marked rarefying osteitis, which I have interpreted as indicating an active reaction locally about the source of infection, and which active and vigorous reaction is a good sign and constitutes the quarantine station protecting the patient. But this extensive absorption of alveolar bone, as revealed in the roentgenograms, did not take place lately, but years previously; and in all probability, as indicated from the history, for a long period of time these individuals did not have anaphylactic reactions from these processes. In studying the ionic calcium of the blood it was noted that these individuals have a high normal, usually above normal, whereas the individuals suffering from the typical rheumatic group lesions generally had an ionic calcium of the blood, at the time they were suffering from their rheumatic group lesions, which was below normal, frequently considerably below.

I have found one type of rheumatism which appears to be present only in individuals having a pathologically high ionic calcium. Histopathologically, it is quite a different type of reaction from that of the arthritides. It is generally characterized by degenerative, rather than proliferative, processes, which sometimes are revealed roentgenographically by the radiolucency of the bones.

Since it is demonstrated that this quality of anaphylactic reaction to dental infection occurs only in individuals who have had a history of very high defense against streptococcal infections and rheumatic group lesions, we have in the histories of all of the patients, shown in this group, evidence of an overload of dental infection in an individual with a high capacity for reaction, which overload of dental infection was maintained for a long period of time. The effect has seemed to be that inasmuch as one of the first principles of defense is the capacity to reacting to a relatively small quantity of the irritant, these individuals developed so sensitive a mechanism of reaction that when the local barrier began to break down immediately about the infected teeth, those tissues which were most easily capable of developing an exalted reactivity, disclosed the presence of this toxin which had laterally become able to pass into the system, and they have thereby suffered a more or less constant state of exalted reactivity in these very reactive dermal tissues. So far as I know this is the first time this evidence has been observed, suggesting a simple interpretation of the nature of the anaphylactic reaction in these individuals. I have discussed this further from this standpoint in the next chapter on Precancerous Skin Irritations.

In order to study the capacity of toxic substances extracted from infected teeth for sensitizing rabbits to extracts made from the cultures grown from the same teeth, I have inoculated animals with these products with results shown in the chart in Figure 177. Rabbits 789 and 790 were controls; and it will be noted that they did not show skin sensitizations to the extracts from any of these products; whereas, Rabbit 814 showed an anaphylactic reaction to a sodium hydrate extract from the culture grown from the teeth of another patient; and in Rabbits 846, 847, and 848, we find all three rabbits, which have previously been injected with the toxic extract taken from this individual's teeth, were all sensitized and gave anaphylactic reactions to the sodium chloride filtrate to the extract of the whole culture grown from the teeth of this same patient as shown in Rabbit 846; and Rabbit 847 showed a reaction to the sodium hydrate extract from the culture grown from the teeth of this patient, and in Rabbit 848 the same condition. Whereas the tests for the extracts made by all the other methods were negative, these latter two were positive in sixty minutes and lasted for two hours.

Another group of rabbits was tested by using as our extract the toxic substance obtained from some recently extracted infected teeth from several different patients. These showed different reactions to extracts made by different methods. Whereas Rabbit 778 reacted to the extract of the whole culture, Rabbit 780 reacted to the powder obtained from the dehydrated washings, Rabbit 781 to the whole culture and the powder obtained by dehydrating and washing, and Rabbit 779 to the powder and the whole culture.

DERMAL SENSITIZATIONS DEVELOPED IN RABBITS

A. Ear used as Test.

Rabbit No.	Weight	Date of Inoculation 1922	Material	Date of Test 1922	Weight	NaCl			NaOH			Time Factor			Pathological Findings
						Filtrate	Polyvalent	Culture of 1237	Filtrate	Polyvalent	Culture of 1237	15 min.	60 min.	2 hrs.	
846	1205	3–1	Filtered washing	3–7	958	+	—	+	—	—	—	—	—	+	Abscess cecum. Muscle atrophy. Paralysis of muscles, small intestines?
847	1060	3–2	Filtered washing	3–7	983	—	—	—	—	—	+	—	+	+	Emaciation. Muscle atrophy.
848	962	3–2	Filtered washing	3–7	715	—	—	—	—	—	+	—	—	+	Emaciation. Muscle atrophy.
814	948	1–4	Washed culture	2–9	905	—	—	—	—	—	+	—	—	+	Pneumonia. Abscesses kidney. Cysts ovaries.
789	791	1–20	Culture	1–26	849	—	—	—	—	—	—	—	—	—	No gross pathology found.
790 Control	1040	1–26	Filtrate from culture, intra-muscular	1–26		—	—	—	—	—	—	—	—	—	No gross pathology found.

B. Abdomen used as Test.

Rabbit No.	Weight	Date of Inoculation 1922	Culture No.	Date of Test 1922	Weight	Rt. Side Abdomen			Lf. Side Abdomen			Control	Time Factor				Pathological Findings
						Powdered organisms	Powdered washing	Whole culture	Powdered organisms	Powdered washing	Whole culture		10 min.	60 min.	2 hrs.	3 hrs.	
778	1035	1–10	572 575	1–19	998	—	—	+	—	—	—	—	+				No gross pathology found.
780	1389	1–10	572 574	1–19	1290	—	+	—	—	—	—	—	—	—	+	+	Purulent arthritis, knee joints.
781	854	1–10	572 575	1–19	772	—	—	+	—	+	—	—	—	—	+	+	No gross pathology found. Coccidiosis.
779	1337	1–10	572 574	1–19	1221	—	+	—	—	—	+	—	—	—	+	+	No gross pathology found.

FIGURE 177.

SUMMARY AND CONCLUSIONS.

In summarizing these studies of sensitization we desire to present the above data as a preliminary report, for much of the information is not ready for interpretation. Some important facts, however, should be noted. In the first case presented with acute inflammation of the nose, throat, lips, and eyes, the extract which was taken from the tooth and which produced such violent reactions in the patient in thirty seconds to two minutes, produced practically no reactions in any one of six members of the staff treated similarly at the same time, which clearly indicated that we were dealing with a specific reaction.

From these data we are led to conclude:

(1) That teeth contain substances other than bacteria to which the individual may become sensitized, and which substances may, in addition, have strong toxic properties.

(2) The evidence here presented suggests that dental infections are capable of producing in an individual a state of anaphylactic sensitization, which condition may entirely and apparently permanently disappear with the removal of the dental infections. These disturbances may occur in dermal tissues, mucous membranes of the nose and throat, lacrimal tissues, mucous membranes of the bronchioles and air passages, as asthma, and the mucous membranes of the digestive tract and a number of other types of tissues.

CHAPTER XXXI.

PRECANCEROUS SKIN IRRITATIONS.

PROBLEM: Are there relationships between precancerous skin irritations and dental infections?

EXPERIMENTAL AND DISCUSSION.

In the preceding chapter the researches disclosed that dental infections may produce in individuals very marked anaphylactic reactions in various tissues of the body. It was also revealed that there is a relationship between the dental infection, the ionic calcium of blood, and the patient's history of a quite complete absence of rheumatic group lesions, and that this condition developed only in individuals having a normally high defense against streptococcal lesions. A frequent site of these lesions was shown to be the skin which is one of the first tissues to react to anaphylaxis. This has led us to a consideration of some of the types of skin lesions which have tended to recur and persist, and in time, occasionally, or in some types frequently, have taken on premalignant or definite malignant tissue types.

Before proceeding with this discussion, I want to forestall misapprehensions and misrepresentations which are very likely to be unintentionally made. I am endeavoring to be very careful not to say that dental infections have been shown to be the cause of cancer. I am trying to illustrate that since cancerous growths develop in chronically irritated tissues, the data I am here presenting suggest only that dental infections may, in this indirect way, be contributary to these states of irritation.

Figure 178 shows such a case. This patient had suffered for months from a lesion in the skin of her nose which had been diagnosed as a skin cancer. The roentgenograms of the teeth of this case are shown in Figure 179. It will immediately be noted that this individual had extensive areas of absorption for a long period of time (for thirty-four years as evidenced by the history) and at fifty-two years of age she is developing this persistent lesion on the side of her nose. It has tended to fluctuate, varying in severity but never entirely disappearing, usually carrying a thick angry looking scab. We prepared a note for her, directing her to

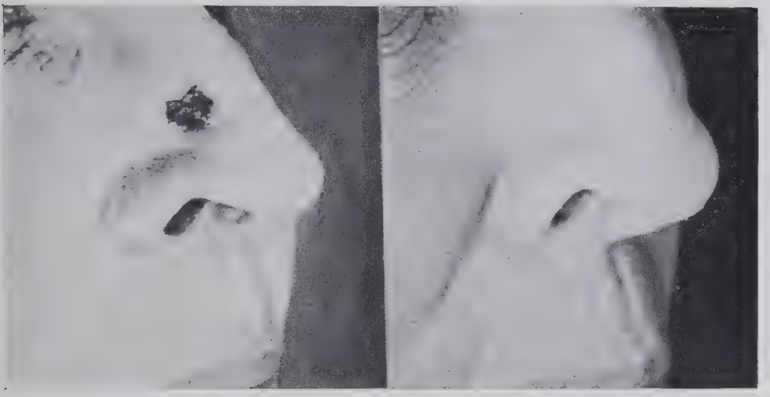

FIGURE 178. SKIN CANCER OF THE NOSE AND ITS APPEARANCE THREE WEEKS LATER AFTER REMOVAL OF DENTAL INFECTIONS. SEE TEXT.

a cancer specialist for its treatment with radium. Almost immediately following the obliteration of her dental infections the red border surrounding it disappeared and it showed evidence of rapid healing. B is a photograph of the lesion three weeks after the making of the photograph shown in A. Her nose cleared up so completely that, as shown in the picture, it was difficult to detect where the original lesion had been. The lesion remained healed for five months when it showed slight tendency to return, at which time she was taken to the cancer specialist who gave it two treatments with radium, since which there has been no recurrence.

We shall not presume to interpret this history, but present the suggestion that if this patient was sensitized to her dental infection in such a manner as were the individuals shown in the preceding chapter, it is not impossible, nor even improbable, that the dental infection had direct relation, whether as a primary or as an additive factor, in the etiology of the lesion on her nose. If it may be that the state of abnormal cell proliferation is due to liberation of some toxic substance from the focus, set free in the system that has a high capacity for reaction to it, taking on a state of sensitization, it is not impossible that an additive factor may thereby be furnished, if not a primary causative factor, in the development of a neoplastic proliferation, in support of which suggestion I will present the following.

When these individuals are sensitized, for this individual was suggested to be from her dermal reaction, they take on a state in which, when the extracted toxin is added to a slight scarification

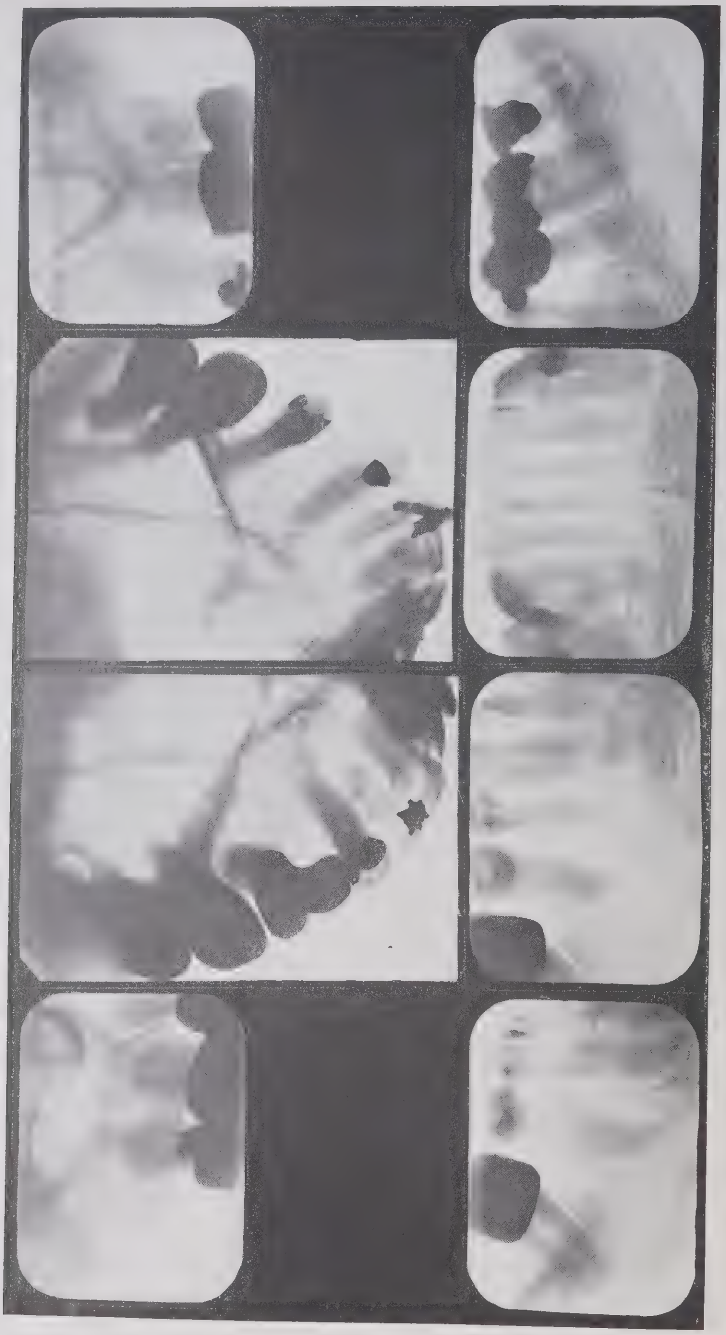

FIGURE 179. ROENTGENOGRAPHIC RECORD OF THE TEETH OF THE PATIENT SHOWN IN FIGURE 178.

of the forearm or introduced in solution into or just beneath the external layer of the skin, there occurs frequently, in a very few seconds, and practically always, in a few minutes, a vascularization with a very marked dilatation of the capillaries. When tubes carrying such a sensitizing antigen are placed beneath the skin of a rabbit, as in its ear, and removed in a few minutes, it is found that there is a very rapid migration of leucocytes to the zone. Carrell has shown that leucocytes contain an activating substance capable of inducing cell defense and proliferation comparable to the activation of embryo and tissue juice. This suggests as a possibility that dental infections may produce irritations either in the epithelial tissues, as shown in these various skin reaction cases of the preceding chapter, or in mucous membranes, also shown in the preceding chapter; and if, as is frequently the case with these lesions, they remain located in a given spot for a long period of time, it may be possible that a hypersensitiveness, a part of which constitutes a marshalling of the leucocytes, may be one of the important steps in the development of neoplasms. Possibly related to this will be found the development of abdominal cysts, many of which we show produced in rabbits in Chapter 62 of Part Two. In the Chapter on Lesions of the Digestive Tract in Part Two (Chapter 65) we recite a number of cases of lesions of the alimentary canal, chiefly the stomach, which seem directly related to dental infections, inasmuch as chronic lesions, as stomach ulcer which had been recurring for years, have entirely disappeared and have remained absent for a number of years following the removal of the dental infections, and the teeth from which cases, when cultured, produced in rabbits, as shown in those chapters, many instances of stomach ulcer and perforations of the stomach and intestines. We will discuss this phase of this problem further in our general interpretations.

I have said, "*if* she was sensitized." In order to determine this I made extractions from her extracted teeth and tested both of these and also an extract from the organisms grown from her teeth in culture media and found her to react positively to the dermal test and maximum positive in twenty-five minutes, which disappeared in three hours. The same antigen used on control individuals was negative. It is my interpretation, therefore, that she was, as a matter of fact, in a state of allergic sensitization to the toxic substance being developed in her dental infection.

I am quite familiar with the fact that there is divergence of opinion as to whether there is any hereditary tendency associated with cancer; and, indeed, the evidence is far from conclusive that there is such. If, as I have suggested, sensitization processes may tend to contribute to precancerous irritations, it would be entirely possible to explain the association of these irritations in families without requiring as a premise that the cancerous condition, *per se*, is transmissible. To illustrate: Individuals do not transmit to their posterity, periodontoclasia, or so-called pyorrhea alveolaris. However, it is a condition which is found to involve all the members of some families and be absent in all the members of other families. The factor that seems to be transmissible in this case is an exalted or highly efficient capacity for reaction against the presence of an irritant; and, since all the members of the family have been blessed with this high defense in common, and since all individuals tend to have irritating deposits about the teeth, and irritating food packs about improperly spaced teeth, or those with destroyed contact points, the irritants to which to react are practically universal. The removal of the irritants and prevention of their recurrence will usually be all that will be necessary in these individuals to prevent the development of a local disturbance spoken of as periodontoclasia, or pyorrhea alveolaris. Similarly, since only individuals with a normally high defense reacting against a persisting toxic antigen, seem to develop this state of sensitization, it would not be strange if different individuals in the same family developed such similar reactions to similar irritants. This may be the explanation for the phenomena which are exhibited in the chart shown in Chapter 65 in which it will be seen that the patient has stomach irritation, sluggish liver, and acute digestive disturbance, from which disturbance one of his brothers is also suffering, and also both his father and mother. It is also important that his father's father and one of his father's brothers died of cancer of the stomach at sixty and sixty-three years of age respectively, and his mother's mother of a chronic stomach disturbance, not identified, at the age of sixty-four. The history of this family shows a marked tendency to periodontoclasia in each the patient, two of his brothers, and his father. This, as we have shown, is a disturbance which tends to develop in individuals with normally high capacity for reaction. They, therefore, would also have a high capacity for reaction to other sources of irritation, not necessarily of dental origin, though readily from that source, which might express themselves as sensitizations. If, then, there be an inheritance of a tendency to low defense of stomach tissue, this sensitization process could readily attack that tissue and in this definite but indirect way, either precancerous or cancerous conditions may possibly be associated and related when they occur in different members of the same family, as here shown.

SUMMARY AND CONCLUSIONS.

Since more individuals lose their lives from cancer of the stomach than from cancer of any other type of tissue, and since dental infections are shown in the chapter referred to, to be directly related to so many cases of acute and chronic digestive tract disturbance, we should be exceedingly careful that dental infections are not permitted to become a predisposing factor, for it has been abundantly shown that cancer of the stomach tends largely to develop in the scars of healed ulcers. Until we have more knowledge as to the extent of anaphylactic reactions in the many lesions produced and aggravated by dental infections, we cannot with safety undertake to interpret the full role which dental infections play in acute, chronic, or malignant processes. The evidence, however, is sufficient to suggest extreme caution in matters of prophylaxis.

The evidence available suggests:

(a) That dental infections may produce localized anaphylactic reactions, as irritations of the skin and mucous membranes.

(b) That these sensitizations may develop into precancerous conditions.

CHAPTER XXXII.

RESEARCHES ON DENTAL INFECTIONS AND CARBOHYDRATE METABOLISM.

PROBLEM: What, if any, is the relationship between dental infections and carbohydrate metabolism?

EXPERIMENTAL AND DISCUSSION.

By relating the lesions, which occur in other parts of the body in association with acute and chronic gingival infections, we have an opportunity for securing direct information and also suggestions as to what may be the causative factors producing both the oral and the systemic disturbances. I have shown in Figure 131 Chapter 20 (showing relation of blood chemistry studies to systemic involvements like diabetes, etc.) and also in other places that certain groups of disturbances tend to be associated, as, for example, a pathologically high ionic calcium of the blood, low alkali reserve, low respiratory coefficient, extensive gingival involvement with alveolar absorption, high blood sugar (hyperglycemia), sugar in urine (glucosuria), tend to be associated, and that this group tends not to have deforming arthritis or acute rheumatic group lesions; whereas the group, with the other extreme of divergents from normal, does tend to have susceptibility to the rheumatic group lesions. It is therefore suggested that the associated factors must be operating in these two conditions.

I have, accordingly, undertaken a series of researches to establish, if possible, some of the mechanisms herein involved. Since the presence or absence of sugar in the urine is dependent in diabetes mellitus upon a disturbed carbohydrate metabolism, it is very probable that the mechanism controlling that process is directly related to the various modifications in the two distinct types of lesions. It has been known for some time that the surgical removal of the pancreas always tends to produce typical diabetes with death in the animal, in a few weeks. The rise in the sugar in the blood is constant as it is also in the urine. This has led many investigators to a search for the specific hormones, which, it was interpreted, must be developed by the pancreas, controlling the metabolism of the carbohydrates. Very erratic but occasionally definite evidence was developed which indicated that the process was a complicated one. Recently Banting,[17] Best, Collip, and Macleod have succeeded by a special technic in isolating a substance from the pancreas, which when injected into normal animals, definitely and rapidly lowers the blood sugar, and which, when administered to depancreatized animals, immediately reduces their blood sugar to, or below normal in accordance with the dosage. They have demonstrated that this substance is a product of the islets of Langerhans. When extracts are made of a whole adult pancreas, a quantity of the specific substance, to which they have given the name insulin, is secured in varying amounts, as judged by the effects upon animals when making injections with this material.

It seems very probable from experimental data that the differences in these reactions are not due entirely to differences in amounts of insulin, but in large part to differences in the amount of some other substance which probably is extracted from the same pancreas, and which excites an influence in the opposite direction. In other words, when carbohydrates are taken into the body they are at first formed into sugars. In a normal individual this sugar is stored in the liver as glycogen and a liberal quantity is carried in the blood to the various tissues of the body where it is oxidized in the process of work and is the principal body fuel. In diabetes the body has lost the capacity for burning this fuel and it accordingly accumulates in the blood. In that state the body has lost the capacity for storing it as glycogen in the liver. Nature also stores away the excess by adding additional carbon, depositing it in the tissues as fat. This fat may be called upon in the absence of fuel, and by oxidizing its carbon atoms from the molecules in pairs, reduces it from fat to glycogen, glycogen to sugar, sugar to butyric acid, and finally carbon dioxide and water. In diabetes the body cannot completely burn up these sugar compounds, does not reduce them lower than a butyric acid, which latter then develops into the acetone bodies which, when they accumulate in the system, become very toxic. In Chapter 64 on Arthritis we record many rabbits in which we have produced typical various types of rheumatism by the injection of cultures from dental sources, usually from patients suffering from rheumatic lesions.

On the theory that the pancreas furnishes two opposing hormones which produce an equilibrium in accordance with their relative amounts, one of which is insulin, I have wondered if it might not be true that another hormone, not as yet isolated, might be one of the substances which is directly attacked and destroyed by the types of infection which produce acute chronic rheumatism; and if in other patients the dental infection or its toxins injures the functions of the islands of Langerhans, thereby diminishing the supply of insulin. It has been shown that, whereas the pancreas of mammals contains two distinct types of secreting cells, one of which constitutes the islets of Langerhans, some of the mammalia have these two tissues separated into different organs, as, for example, in some of the fishes, particularly the scallop.

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[17] See bibliography

I have shown in Chapter 20 that cultures taken from dental infections are capable of greatly changing the percentage of sugar in the blood of animals and also the development of a glycosuria, which condition recovered in a few weeks, but which was reproduced in the same animal by reinoculation of a culture from the same patient, which patient was suffering from diabetes. We have, accordingly, repeated this experiment, having in mind especially the structural changes in the pancreatic tissues and in carbohydrate metabolism. We have also undertaken to modify these effects by injecting the animals with the opposing enzyme or hormone, assuming that two exist, which are in apposition in the affects. The results of these studies will be published later. These researches are in progress and have opened up an entirely new approach to a very important problem, since in a large number of our patients there has been a marked improvement in the glycosuria and the hyperglycemia following the removal of dental infections.

SUMMARY AND CONCLUSIONS.

Dental infections may produce marked changes in carbohydrate metabolism and probably structural and degenerative changes in the islets of Langerhans of the pancreas, with the production of hyperglycemia and glycosuria.

CHAPTER XXXIII.

MARASMUS.

PROBLEM: Why do people with rheumatic group lesions tend to be underweight?

EXPERIMENTAL AND DISCUSSION.

Few, if any, of the symptoms of rheumatic group affections are so constantly found as that of marasmus. This condition of progressive wasting and emaciation may range from 10 to 25 per cent in ordinary cases, to 35 to 40 per cent in extreme cases.

The patient shown in Chapter 64 has increased in weight from 72 to 111 pounds, an increase of more than 50 per cent of her weight at the time her dental infections were removed, her normal prior to her affection being about 130 pounds. She had, accordingly, lost nearly half of her original weight. A culture was taken from one of her infected teeth and inoculated into the rabbit shown in Figure 180. In four days' time this rabbit reduced in weight from 1381 to 1105 grams, a loss of 276 grams, approximately 20 per cent. The amount of culture injected was 1 cc. of a 24 hour growth. (Sixteen drops, not quite a teacupful.) B shows the marked tissue atrophy about the eyeball which has shrunken so as nearly to fill the orbit.

It is not, however, necessary that even this quantity of organisms be injected, for even the washings of a crushed tooth will produce this extreme emaciation. A patient presented whose principal lesion was his great emaciation. He stated that he felt fairly well, nothing particularly wrong except that he could not regain his weight, which he was progressively losing. He had several dental infections, largely the result of former pockets of active periodontoclasia, now harboring a mixed infection. One of his teeth was crushed, washed, and centrifuged. The clear solution was inoculated into the rabbit shown in Figure 181. This rabbit lost in weight from 1430 grams to 843 grams, a total of 41 per cent in 16 days. We have estimated by counting the number of organisms and weighing a quantity of them, that the actual organisms inoculated into this rabbit would be approximately one millionth of a gram.

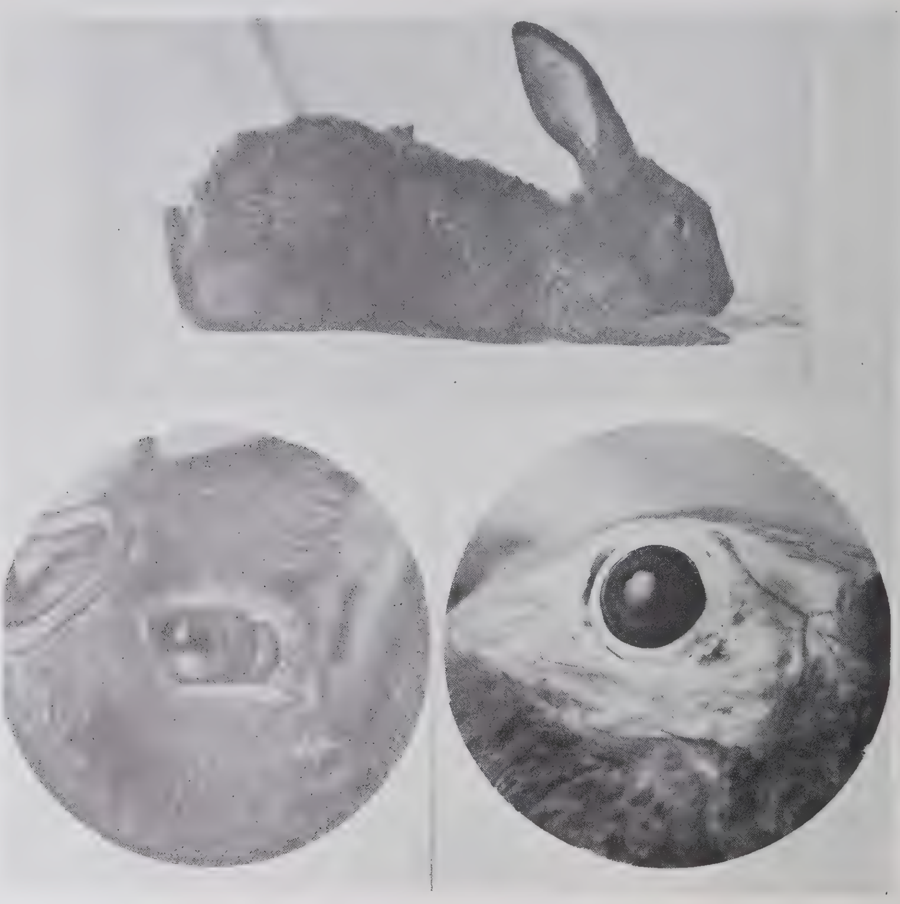

Figure 180. Marked tissue atrophy produced by injection of a dental culture, twenty per cent in four days. No cleft between eyeball and socket.

To test this matter still further, we have passed the washings from crushed teeth through a Berkefeld filter and have injected the bacteria-free solutions into rabbits and have produced typical marasmus. We have shown elsewhere, in a discussion of the effects of the toxic substances contained in infected teeth upon experimental animals, that there is a marked loss in weight following their injection. For example, in thirteen rabbits inoculated, intravenously, with filtered washings of teeth, where the death was spontaneous, the average length of life was 5 days, the average loss per rabbit was 191 grams, and the average percentage loss in 5 days was 19, or almost 4 per cent per rabbit per day.

In chapters 59 to 112 there are shown many patients with various types of rheumatic group lesions: muscles and joints,

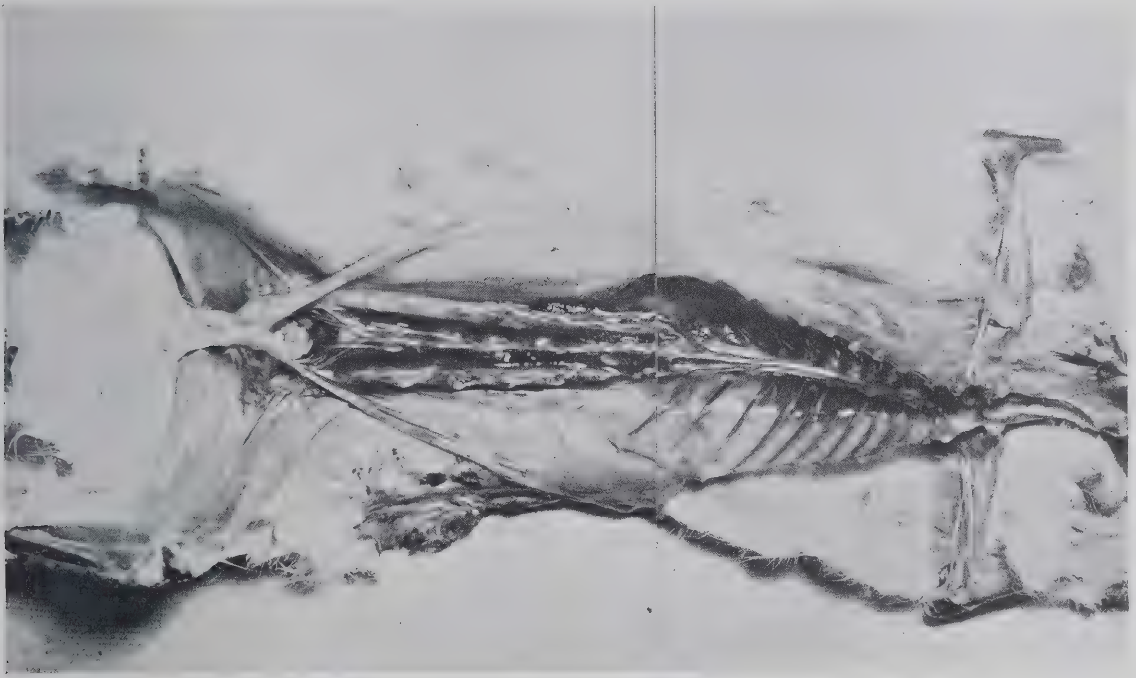

FIGURE 181. TYPICAL MARASMUS IN RABBIT INOCULATED WITH CLEAR WASHINGS FROM CRUSHED TOOTH OF PATIENT. RABBIT LOST 41 PER CENT IN SIXTEEN DAYS.

heart, nervous system, digestive tract, etc. Accompanying these practical cases are shown animals inoculated in various ways with various cultures of dental origin and with toxic substances extracted from teeth, and the percentage of their loss of weight at the time they were chloroformed, or died.

In a group of 667 successive rabbit inoculations, some with cultures and some with filtrates of cultures, and many with filtered washings from crushed teeth, therefore bacteria-free, 33 1/3 per cent, or 220, lost in weight from 10 to 30 per cent in a few days or weeks immediately following the injections; and 8.7 per cent lost from 30 to 50 per cent in weight; 13.6 per cent gained from 10 to 30 per cent, and 3.6 per cent gained from 30 to 50 per cent. It will be seen immediately that, in this group of rabbits selected serially, irrespective of the type of experiment, nature of culture, or method of inoculation, there is a very much larger percentage of rabbits having a loss, than a gain. In other words, 42 per cent of the animals lost more than 10 per cent in weight in a few days or weeks under which they were in observation, extending from that to 50 per cent; whereas only 17 per cent gained

PER CENT LOSS OR GAIN IN WEIGHT AFTER INOCULATION OF 667 RABBITS

Loss		Gain	
10-30%	30-50%	10-30%	30-50%
33.3	8.7	13.6	3.6

FIGURE 182.

more than 10 per cent. (See Figure 182.)

When teeth are planted beneath the skins of rabbits, they often show a loss of weight within 24 hours; and in 100 consecutive plantings for various types of experiments, the loss of weight per rabbit per day amounted to 18 grams, which was 1.4 per cent. In chapter 17, we refer to a strain growing in a patient's teeth six of which teeth were tested on sixty rabbits by planting one of them beneath the skin, which in every instance killed the animals in from two to ten days, with an average loss of weight of 26 grams per day per rabbit, or 15 per cent per rabbit and 2 per cent per day per rabbit, an average total of 205 grams per rabbit. In Chapter 18, we have illustrated two rabbits, full brothers, kept on the same diet, one of which gained continuously and the other began immediately to lose in weight, after being injected with the washings from a crushed tooth.

In this connection it is of interest and important to note that, invariably as the ionic calcium of the blood is reduced by the presence of the implanted tooth, the animals lose in weight. This is clearly shown in the chart in Figure 134, Chapter 20, in which a series of rabbits is shown to demonstrate the changes which take place in the calcium and thrombin of the blood in the presence of dental infection. In these the ionic calcium was very seriously depressed, and, as shown in Chapter 20, the evidence is very strong that this is a fundamental part of the process of bacterial overwhelming. It is also of interest to note, however, that the loss in weight is not exactly proportional to the loss in ionic calcium.

The data, that are rapidly accumulating, strongly suggest, if they do not indicate, that infected teeth contain, in many instances, a toxic substance or substances capable of producing very many grave disturbances in metabolism, only one of which is the universal expression as marasmus. Since it is so common a symptom of chronic dental infections, that patients having them are underweight and that they tend so frequently to gain in weight after the removal of their dental infections, together with the fact that whether we inject the filtered washings from the teeth or plant an infected tooth beneath the skins of rabbits, this effect generally quite rapidly obtains, we are, therefore, led to the presumption that these toxic substances are directly related to that symptom.

SUMMARY AND CONCLUSIONS.

(1) A study of our clinical records shows that a large percentage of the patients suffering from rheumatic group lesions are from 10 to 30 per cent under weight, and that they tend to return to, or nearly to, their normal within a few weeks or months following the removal of their dental focal infections.

(2) When the same tooth which, when removed, produces such a change in the patient that he or she returns to his or her normal weight, is placed under the skin of a rabbit, it nearly always loses in weight, not infrequently 20 per cent in a few days.

(3) When cultures grown from infected teeth are inoculated into rabbits, whether intravenously, subcutaneously, or intraperitoneally, they tend to lose in weight though usually not so rapidly as when an infected tooth is placed beneath the rabbit's skin.

(4) Filtered washings from infected teeth frequently cause very marked reduction in weight.

We are, therefore, led to conclude:

> **That dental infections, when they affect the patient systemically, frequently, if not generally, produce a depression of that individual's weight; and that marasmus, whether mild or severe, may be considered one of the diagnostic symptoms in studying the relation of dental infections to general health.**

CHAPTER XXXIV

PREGNANCY COMPLICATIONS.

PROBLEM: Do dental infections have a bearing on pregnancy complications?

EXPERIMENTAL AND DISCUSSION.

We have seen in Chapter 21 that one of the conspicuous overloads, which contributes to susceptibility to rheumatic group lesions, is pregnancy; and having noted that so many of our patients either presented with the development of these lesions during pregnancy and lactation, or with a history dating to that period, we were led to study to see whether or not dental focal infections may have an injurious effect upon that state.

It has long been known that the administration of toxic substances to pregnant animals has tended to injure the fetal forms often before the parent was seriously affected. This has been the basis of a procedure for producing a miscarriage by the use of such chemicals as the lead compounds. In our experiments we have found that when infection was introduced into pregnant rabbits, that infection produced more profound effects than when introduced into non-pregnant rabbits, and that this injury expressed itself in fetal forms before it did in the mother. Is it not probable then, that dental infections may have somewhat of the same effect upon human expectant mothers? This is a fact of very great importance in all the campaigns which have to do with the better care of expectant mothers and with the prenatal care of infants, and urges strongly that a part of all government co-operation shall include the placing of the expectant mother's oral cavity in a condition free from focal infections, both for her own safety and for the safety of her offspring.

This is doubly true for the following reason: In pregnancy the demand for calcium is greatly increased, both for the general metabolic processes and for the new fetal form. It has also been shown in the preceding chapters that the presence of the dental infection furnishes a toxic substance which tends to combine directly with the ionic calcium of the blood, and besides produces

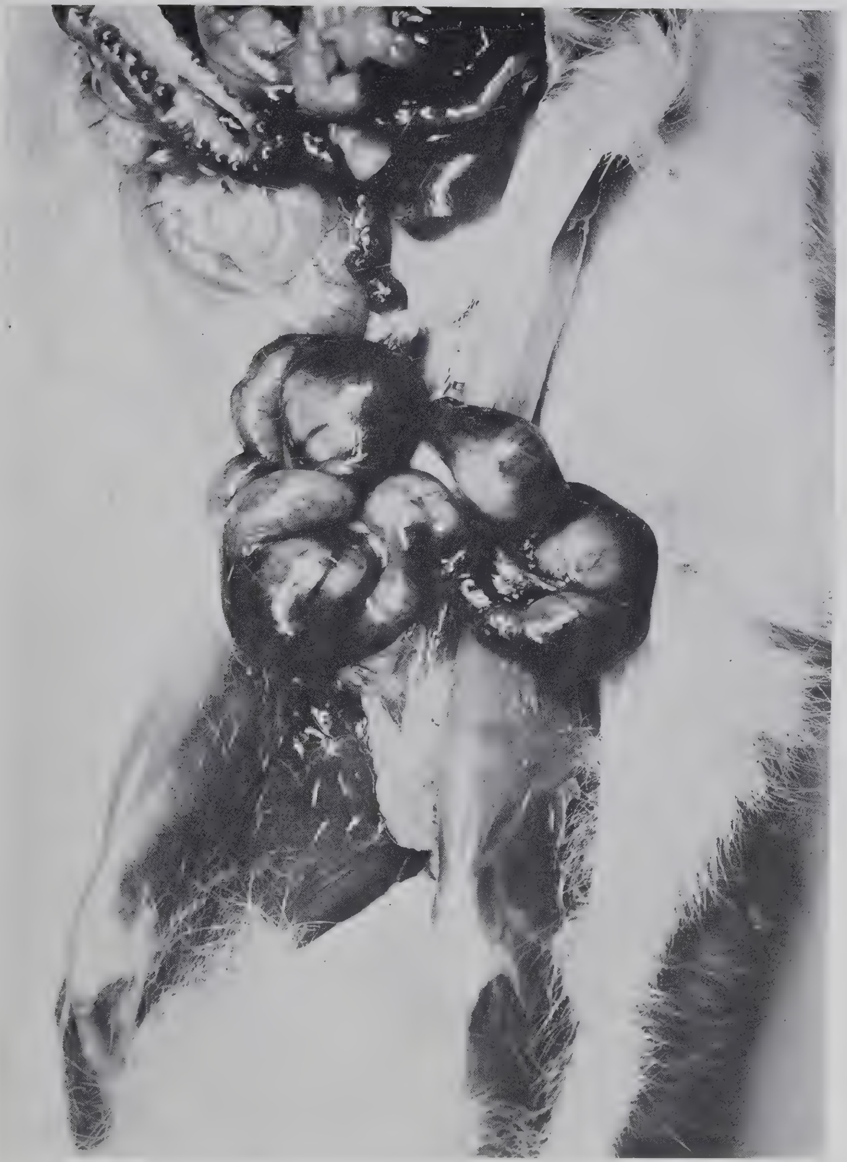

FIGURE 183. DEAD FETAL FORMS FOLLOWING INJECTION OF 1CC. OF DENTAL CULTURE.

a toxic factor definitely reducing the available ionic calcium. In practically every instance where a tooth is planted beneath the skin of a rabbit, as we have shown, the ionic calcium of the blood is reduced. If, then, the expectant mother is to be deprived of her available ionic calcium by having its effectiveness destroyed in the circulation, by being attached to a toxic factor, supplied by the dental infection in addition to the increased demand for that ionic calcium, we have two important contributing factors to a general lowering of defense, to make the third factor more serious and dangerous: namely, the direct injury of the foreign toxin produced by the dental infection upon the fetus. It is not an uncommon clinical experience to have premature labor pains develop with the onset of a dental abscess; and while it is not possible, in a given case, to say what the relative importance of different contributing factors has been, it is not improbable that many miscarriages or prenatal injuries, many of which latter are permanent, may have their origin directly in the obscure and unsuspected dental infections.

We, accordingly, injected cultures from dental origin into pregnant rabbits similarly as in our other studies. Figure 183 shows a dissection of such a rabbit, in which five nearly developed fetal forms are dead and undergoing decomposition from the injection into the ear vein of 1 cc. of a 24 hour growth of a culture from a tooth.

As a further means of study of this problem, we have planted pieces of infected teeth beneath the skin of pregnant rats in order that we might, if possible, observe the effect on both the mother and the offspring. The period of gestation in rats being three weeks, makes a very short experimental period, and it is difficult to determine the progress of the period of gestation by the appearance of the animals. There has been evidence of the premature birth of the offspring within a couple of days after the planting of the piece of infected tooth.

SUMMARY AND CONCLUSIONS.

We would, therefore, summarize these studies as follows:

(1) These researches have shown that, in animals, infections from dental origin may have a very far-reaching effect on both the expectant mother and her fetus, which latter may be prematurely expelled or may be rendered lifeless.

(2) Inasmuch as a large number of our serious cases of rheumatism, heart, and kidney involvements, have their origin at the time of pregnancy in humans, in which cases our clinical histories show that there have been present extensive dental focal infections, it is suggested as important, if not imperative, that expectant mothers shall be free from dental focal infections, both for their own safety and efficiency and for the continued vitality of the fetus.

CHAPTER XXXV.

SPIROCHETE, AMEBA, AND OTHER NON-STREPTOCOCCAL INFECTIONS.

PROBLEM: Do other organisms than streptococci enter the human system through dental infections?

EXPERIMENTAL AND DISCUSSION.

The conclusion that has been reached in nearly all the recent reports on dental infections, bears out the evidence in the preceding chapter, to the effect that, in general, dental infections may be considered as streptococcal or diplococcal infections. Our studies are revealing that while dental infections are practically always a part, and usually the all important part of the involved microörganisms, there are present with the streptococci, frequently, other types of microörganisms which have a very serious effect on the host. These may include either protozoa or bacteria or both. We would discuss two of the protozoa infections first.

In Figure 184 we have a large abscess on the neck which had resisted treatment for many weeks. A bacterial examination of its contents, shown in B, disclosed a large number of amebæ. The history of the case revealed that a lower left first molar had abscessed with a fistula developing below the mandible, which later developed into a chronic abscess which persisted after the extraction of the tooth. C shows the mandible where the tooth was extracted. The use of succinimid of mercury, a good amebacide and disinfectant, as a wash and pack, produced the immediate healing of the abscess.

We do not know to what extent spirochete forms from the mouth enter the human body. We are coming to believe that they do so much more often than has been realized.

Figure 185 shows a rabbit's knee which has developed a huge tumor-like mass which, when opened, proved to be almost pure culture of spirochetes. A shows a large abscess in the thigh of the rabbit, from which a nearly pure culture of spirochetes and fusiform was obtained, as shown in the smear in Figure B. The rabbit was inoculated intraperitoneally with the washings from a periodontoclasial tooth of a patient who had been suffering from

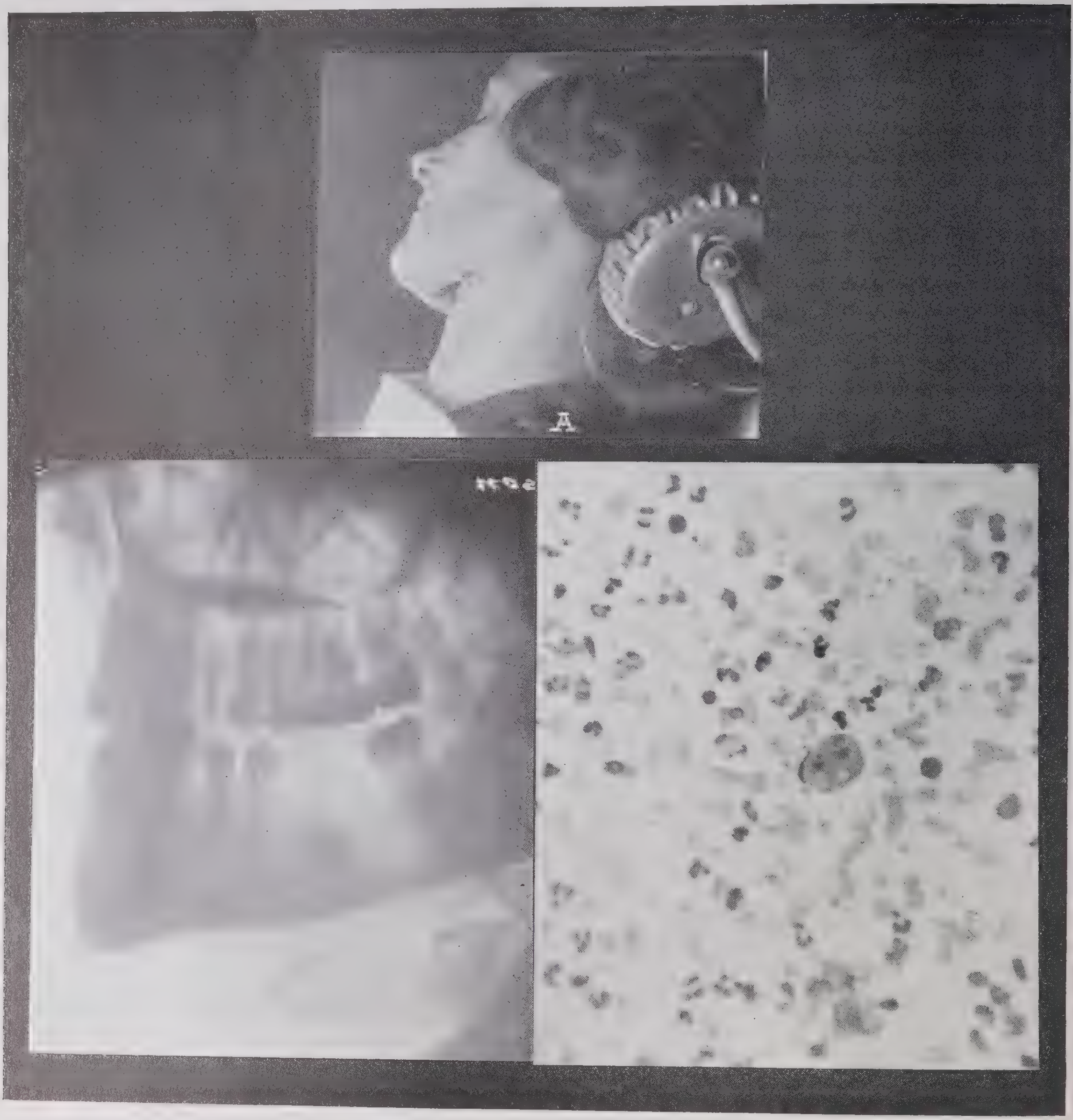

Figure 184. Abscess on neck shown in A; ameba infection shown in B; origin from infected tooth socket shown in C.

an unusual type of neuritis, which was completely relieved by the extraction of the involved tooth. The lesion in this rabbit's thigh contained a culture, apparently, presumably like the culture which we had studied in the pocket beside the tooth before the extraction of the tooth.

The direct influence of the spirochete infections upon the health of the individual may be both severe and rapid. Such a case is shown in Figure 186. This man had lost eighteen pounds in weight

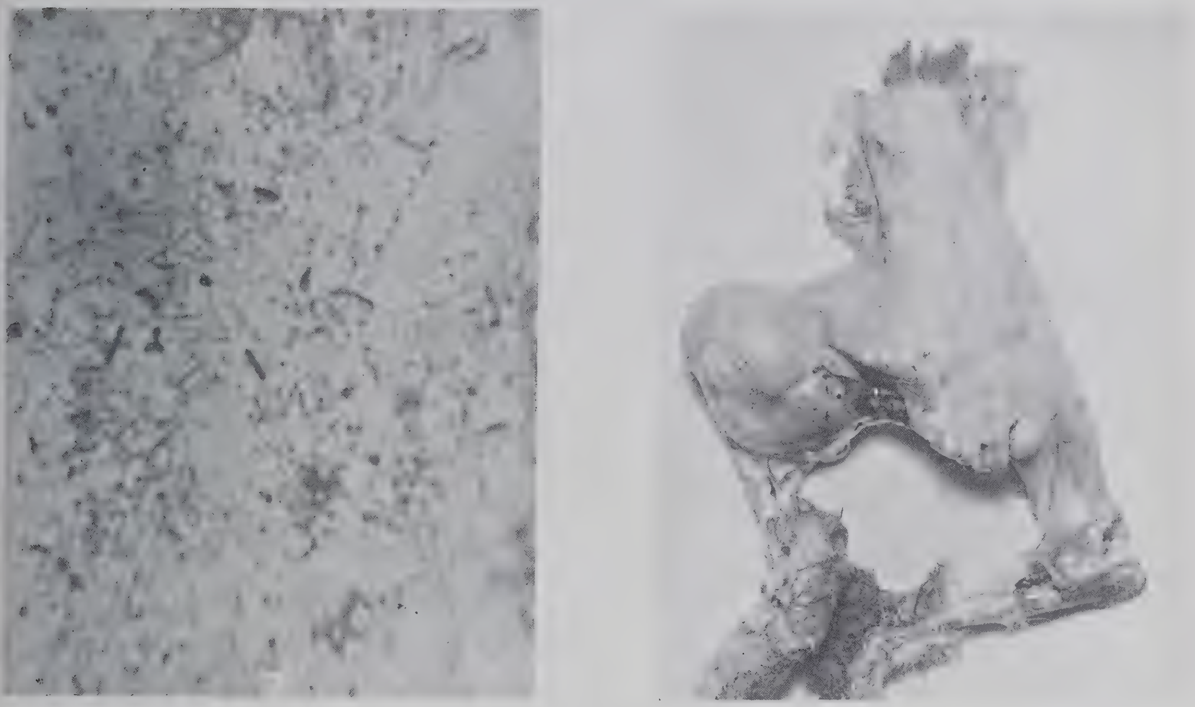

Figure 185. Spirochetal abscess roduced in rabbit in A; B, culture f same.

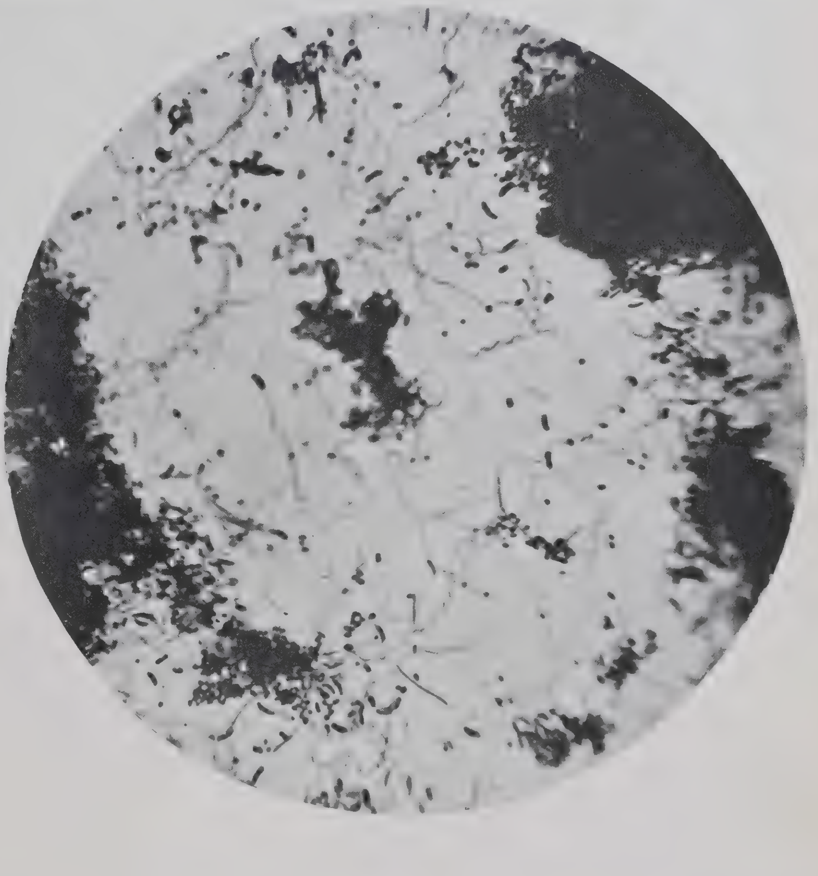

Figure 186. Culture of spiro-hetes from trench mouth, which aused patient to lose eighteen ounds in three weeks. With local reatment he gained ten pounds in wo weeks.

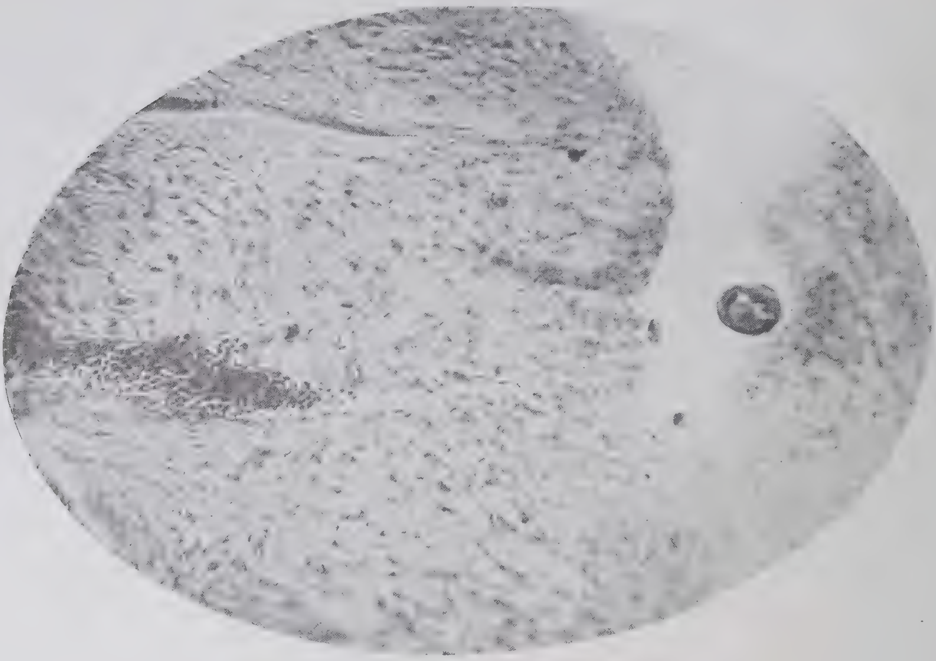

Figure 187. Ameba infection deep in the gingival tissue.

in three weeks' time, and a most thorough medical examination could find no other cause. As an experiment, as well as a wise procedure, in his case because of the extreme painfulness of his gums, the first treatment was by means of packing the selected germicides between the teeth, with the remarkable result that he gained ten pounds in two weeks' time.

Amebæ may penetrate deeply into the soft tissues surrounding peridental involvements, and since amebæ are nearly always present in pockets of periodontoclasia, it is not improbable that they may, at times, penetrate far into the tissues. Figure 187 shows a large ameba deep in the gingival tissue in the neighborhood of a tooth with periodontoclasia.

The infections may also penetrate deeply into the bone adjoining a periodontoclasial infection. Figure 188 shows such a case. The organisms are seen in the haversian canal of the alveolar bone adjoining the pocket of periodontoclasia.

It now seems probable that one of the most important portals of entry for tubercular infection is through the cavities of dental caries of the teeth. From the dental caries they penetrate the exposed and infected pulp chamber, and from this gateway proceed through the lymphatics to the deep and cervical lymph

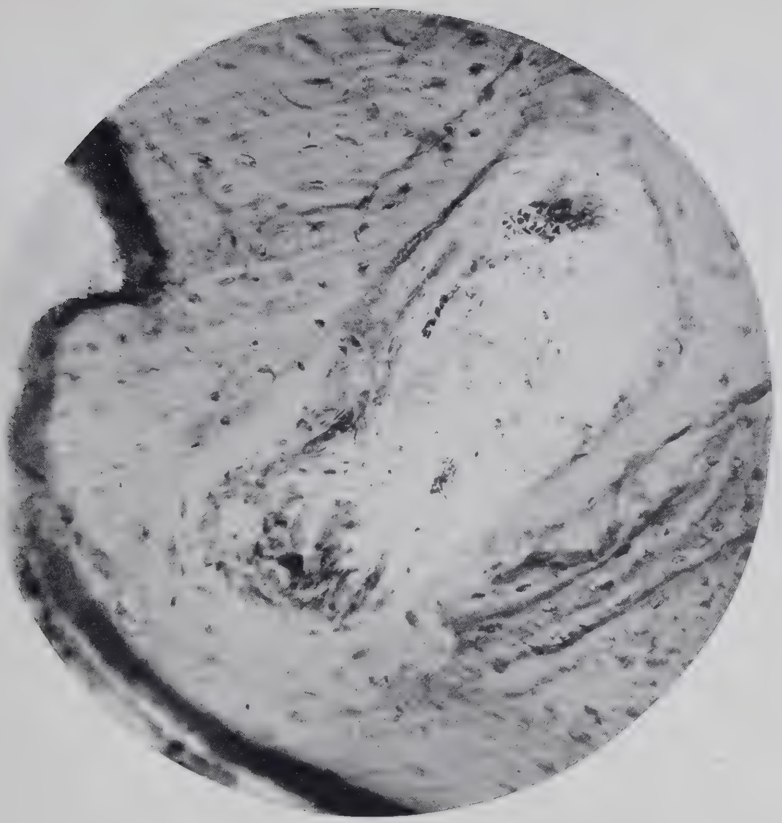

Figure 188. Organisms in an haversian canal, adjoining a periodontoclasia pocket.

glands of the neck. Careful observers in dental practice are constantly seeing the phenomenon of enlarged cervical glands, that have been persisting for periods of time, disappear with the removal of infected teeth. Particularly is this true with undernourished children and their carious deciduous teeth.

Another important phase of this problem is the role of dental caries and the teeth, in the matter of the furnishing of a nidus of infection, which come to be carriers. Particularly is this true of such diseases as scarlet fever and diphtheria. A first requisite for the disinfection of carriers of this type involves a complete eradication of dental infection and dental caries.

But there is another type of infection which is very important and has to do with those involvements, which express themselves through long periods of the individual's life, as recurrences of a one time active process. A typical illustration of this is the following. A patient who had suffered for years from malaria went to a mountain climate to escape the possibility of the mosquito infection; but notwithstanding that she had gone to a malaria free district, she had frequent and definite recurrences of her malaria infection. She returned to Cleveland in midwinter, and in the process of my making her safe from her dental infections by the elimination of foci, after the extraction of her first tooth, she developed a violent and typical attack of malaria fever which was positively diagnosed by finding the plasmodium in her blood. There seems no doubt but that the stirring up of this nidus set free again into her system this organism to produce its cycle. A most remarkable part of her history has been that, whereas these recurrences of malaria had been frequent prior to the removal of her dental infections, she has not had a recurrence in the five years since the removal of them.

It is not yet clearly established whether lethargic encephalitis is produced by an organism of the diplococcus streptococcus group, or by a filterable virus. However, there have been many investigations reported which have tended to establish that it is due to the former. In Part Two on Degenerative and Deficiency Diseases, Their Relation to Dental Infections, I discuss in detail a case of lethargic encephalitis in which it seemed very probable that we were dealing with a type of infection in the tooth, which was directly related to that clinical syndrome, where the tooth was taken from a patient suffering from that disease. In this connection I will state that one of these teeth from this patient placed beneath the skin of thirty different rabbits, produced death in from a day and a half to six days, with one very large rabbit living ten days, and the culture from which tooth, when injected subdurally, produced symptoms strongly suggestive, if not typical of that disturbance. It is also significant that three other teeth taken from this same patient produced similar effects.

The seriousness of these spirochete infections, when they become acute, is common to all practitioners who have had an opportunity for large experience and are generally referred to as Vincent's angina, trench mouth, etc. They may, or may not, show many fusiform. Frequently they are practically pure strains of spirochetes. We will discuss these in their different types and classifications in Volume Three on Diagnosis, Prognosis, and Treatment.

SUMMARY AND CONCLUSIONS.

(1) Our experience with these and other cases suggests to us the great need for very careful study to determine whether or not,

particularly in cases of extensive periodontoclasia, there is an invasion of the organisms of those infective processes, and whether the sensitization reactions discussed in Chapter 30, are not directly produced, in many cases, by toxic substances generated by these other types of organisms.

(2) The evidence at hand strongly suggests that infected teeth are the harbingers of both contagious and infectious organisms which may either attack the host on recurring occasions, or may be transferred by the host who may be non-susceptible and simply a carrier, to susceptible individuals.

(3) Dental prophylaxis becomes imperative both for the safety of the individual and for the community in which he lives.

While the streptococcus seems universally to be present in dental infections in practically all cases of systemic involvement, in addition to this variety the evidence seems to establish that each staphylococci and spirochetes may pass from infected teeth to other tissues and proliferate in localized areas; and, similarly, that when certain mixed strains are injected into experimental animals, localized spirochete infections may develop in their tissues. Systemic involvements from spirochete infections and their localization in experimental animals are, however, relatively rare.

CHAPTER XXXVI.

NUTRITION AND RESISTANCE TO INFECTION.

PROBLEM: Does faulty nutrition, through a deficiency diet, decrease the defense against dental infections?

EXPERIMENTAL AND DISCUSSION.

Few of the overloads so effectually destroy the defense for infection and to such a degree, as does disturbed nutrition. It has been the universal history of the world that wars and famines have been followed by devastating infections. The recent newer knowledge of the nature of foods and their effects upon the developing structures has enormously widened our knowledge of nutritional disorders. The epoch-making work of McCarrison in India, the Melanbys in England, McCollum, Funk, Mendel, Hess, and many others in America, has rapidly established the role of deficiency diets in the long list of physical affections which are more or less common in all lands; and various types of lesions are shown to be very clearly dependent upon the absence of sufficient quantities of accessory food factors, generally spoken of as vitamins A, B, C, and D. McCarrison, particularly, has shown that many of the same diseases can be produced either by deficiency diets or by inoculation with certain infections.

In our extensive studies of the reactions on animals inoculated with different strains of dental infections, we have repeatedly produced symptoms and lesions which resemble in a marked degree those produced by deficiency diets. This research was established to assist in determining the effect of diet in destroying the normal defense of animals and the extent to which the development of infection processes has entered into the clinical pictures of nutritional disturbance, to produce the lesions that are found. Figure 189 shows three views of two rats, same age, one kept on normal diet, and the other on a diet deficient in vitamin B. It is shown here partially paralyzed from polyneuritis, which characterizes the deficiency of this vitamin. It would certainly be expected that animals with nervous systems undermined by this deficiency of feeding would be more sensitive to infection introduced into the animals' bodies. Figure 190 shows

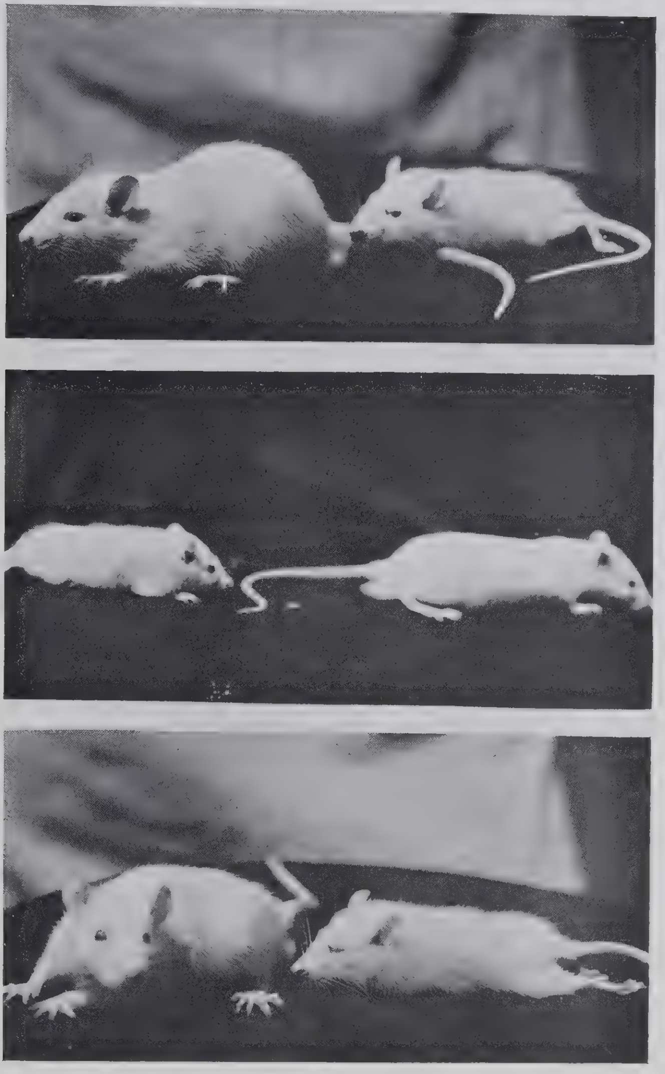

FIGURE 189. Two rats same age, one on normal diet and the other deficient in Vitamin B.

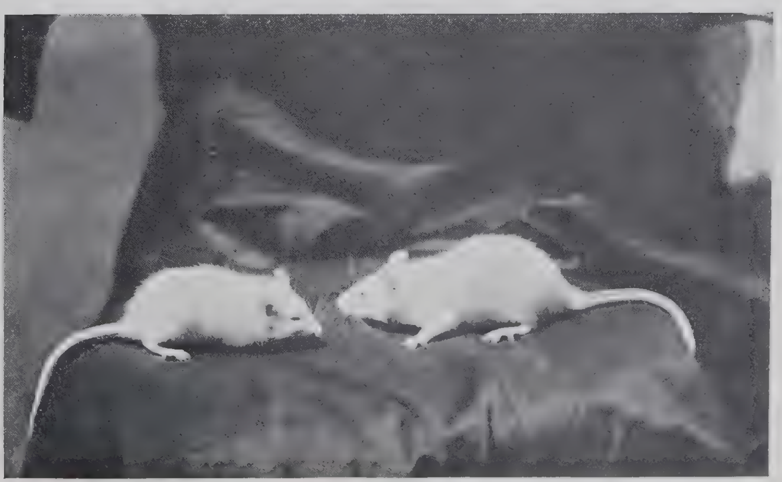

FIGURE 190. The rats on the deficiency diet have also less resistance for infection.

two rats, same age, one on deficiency diet, and the other on normal diet, both of which were inoculated with the same quantity of a strain of dental infection and in which a dose one-third of the tested lethal dose for a normal rat was used.

The newer knowledge of the specific lesions produced by the absence of vitamins A and B has revealed that certain changes in the elements of the blood are in evidence before the physical disturbances appear. Cramer, Drew, and Mottram[18] have shown a progressive decrease in the number of blood platelets following the withholding of vitamin A, resulting in a marked thrombopenia which, they state, is the only constant lesion in deficiency of this vitamin, just as lymphopenia is characteristic of deficiency of water-soluble B. They have also shown that the defense to infection is largely in proportion to the number of platelets, that, when they are reduced below a certain critical number, the animals become an easy prey to infective conditions which develop spontaneously, and which may give rise to secondary anemias, but which disappear, if the condition has not gone too far, on the addition to the diet of vitamin A. McCollum has further divided vitamin A, as understood previously, by limiting its classification to the specific substance, the absence of which produces xerophthalmia. He has characterized as vitamin D, the fat-soluble factor, the absence of which produces the lesions classified as rickets.

We have inoculated rats with given amounts of culture grown from dental infections to determine, if possible, whether in that animal the absence of the vitamins would make them more susceptible to this infection. These results have tended to disclose a very high resistance on the part of the rat for streptococcal infections. We have, however, noted in our inoculations of rabbits that in many instances there was a marked decrease in the platelets and in the thrombin as the result of the streptococcal inoculations, which effects in a degree are as extreme in some instances as the withholding of the specific vitamins.

Vitamin B has been shown by Cramer to be directly related to the production of lymphopenia. Similarly, we have found strains which produced a very marked lymphopenia in animals, whereas other strains produce a very marked lymphocytosis. These are illustrated in the blood counts shown in the chapter on hematological changes in the blood produced by dental infections.

An important phase of nutrition is involved in the typographical climate and isolation of various communities. I shall not enter into a discussion of this problem of nutrition in its relation to localized community conditions. This has been done extensively by such writers as McCollum, McCarrison, etc. I will, however, report the result of a special study that I made among the mountaineers of North Carolina. In these studies, in which I went from home to home on the mountains and also in the valleys, and made tabulations, I found abundant evidence that deficient nutrition was increasing the susceptibility to the rheumatic group lesions. The diet of the mountaineers at that time (Feburary and March, 1919) consisted largely of fat pork, coffee, and the separated grits of the white corn, with a more than liberal use of tobacco, chiefly as snuff, which is painted around the teeth and consists of the powdered stems and leaves. This was far from being a balanced diet. Many of the individuals went for months without milk in their diet, and green foods and vegetables were practically unknown out of season. These individuals showed, in many ways, distinct symptoms of calcium starvation. They were underweight, nervously irritable, and aged young, being frequently more decrepid at fifty to sixty than they should be at seventy to eighty. The most striking feature, however, was the very marked prevalence of rheumatic group lesions, and in many homes I found bedridden sufferers with endocarditis, acute rheumatism, recurring, chronic arthritis, and many cases of digestive and nervous system disturbances. A more careful study of these individuals revealed a very unusual prevalence of dental caries, with striking illustrations of large numbers of broken down teeth, and hence with putrescent pulps and apical involvements, and yet, these frequently existed without fistulæ or evidence of a normal defense and a reaction. They were not maintaining local zones of quarantine about these infected teeth or they could not have been in this quiescent condition.

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[18] See bibliography.

In order to throw some additional light on the problem as to whether or not dental infections are more injurious in individuals on deficiency diets, I have undertaken to reproduce the conditions in animals for study. Different groups of rabbits and rats have been placed in a condition of deficiency in nutrition and then subjected to inoculations and implantations of infected teeth, to determine whether or not those with an unbalanced diet are more susceptible to the infections than the normals. The evidence to date, while, in general, corroborating this viewpoint, does not justify, however, the conclusion that the lowered defense can be charged in large measure to deficiency diet. In many instances the animals with deficiency diet showed remarkable power of defense against infection, though not quite equal to the normals. The results, in general, have been a disappointment in that they have not thrown as large a responsibility on the diet as we had expected. These studies are being continued and will be reported in extended detail later.

The researches on this problem have been in progress approximately a year and the data are being accumulated, which should throw dependable light on this important problem. Rats have not proved to be a suitable animal in which to determine variations in streptococcal defense.

SUMMARY AND CONCLUSIONS.

The data at hand suggest:

(1) That the effects of variations in the diet do not express themselves quickly in specific defense.

(2) That variations in diet by the limitation of various vitamines produce effects which, in general, are similar to those of overload.

(3) Deficiency diets, particularly disturbances resulting in a calcium hunger, tend directly to lower the defense to dental infections.

CHAPTER XXXVII.

THE RELATION OF THE GLANDS OF INTERNAL SECRETION TO DENTAL INFECTIONS AND DEVELOPMENTAL PROCESSES.

PROBLEM: To what extent are the glands of internal secretion related to dental infections and to dental developmental processes?

EXPERIMENTAL AND DISCUSSION.

Probably no department of modern medicine has had a more rapidly developing literature than that of the glands of internal secretion. It is also true that a great deal that has been written has been based upon insufficient experimental evidence, being largely surmises as to the probable role of these various glands. There can be no doubt, however, of the important part which these glands play in all the vital processes, including calcification, metabolism, and immunity. I will not undertake to give an historical review of the literature in its relation to dental problems, as it would be much too voluminous for insertion here. (Its bibliography alone would cover at least one hundred pages.)

I have directed these researches chiefly along the following lines:

(1) The Correction of Disturbances and Disfunctions of the Glands of Internal Secretion of the Patients by the Removal of Their Dental Infections.

(2) The Production of Disturbances in the Glands of Internal Secretion of Animals by the Injection into Their Circulation of Cultures Taken from Teeth of Involved Patients.

(3) The Modification of the Patients' Systemic Involvements from Dental Infections by the Administration of Extracts of These Glands.

(4) The Improvement of the Functioning of the Glands of Internal Secretion by the Mechanical Stimulation Induced by the Movement of the Bones of the Face and Base of the Skull.

We will discuss these under these four heads.

1. THE CORRECTION OF DISTURBANCES AND DISFUNCTIONS OF THE GLANDS OF INTERNAL SECRETION OF THE PATIENTS BY THE REMOVAL OF THEIR DENTAL INFECTIONS.

It is difficult to state which of these glands is most frequently involved. Some are very frequently involved, particularly the thyroid and ovaries. In this great belt lying along the Great Lakes, there is exceedingly little iodin available in the soil and water, and, as a result, thyroid involvements of the various types are very common. It has, accordingly, become necessary to provide iodin for the girls of all this district to make up for this deficency.

Individuals with a defective thyroid due to lack of iodin, readily have that slight disfunction very greatly disturbed and aggravated by dental infection; and the dental infection is distinctly less disturbing to this gland, in the presence of this ample iodin in the food. For example, thyroid involvements from dental infections apparently are very much less frequent among peoples living along the oceans where the spray is drifted inland by the winds, than in this Great Lake belt.

It is now understood that girls are very much more liable to have thyroid involvements than boys, so much so, that the latter are practically free from them unless it be a condition carried forward from the time of a prenatal insufficiency of the mother. Girls and women tend to have the thyroid involvements develop during the periods of physical stress, particularly during puberty and pregnancy. At these times it is very important that they should have an additional supply of iodin if this is not supplied in sufficient quantity in the food. A few grains given every six months will be sufficient to retain the normal functioning of the thyroid.

To test out this important discovery, Marine and Kimball got permission to administer iodin twice a year to the girls of the public schools of the city of Akron, only those being accepted who furnished from their parents or guardians a written request for this treatment. Kimball[19] in his report entitled "The Prevention of Simple Goiter in Man," published in the American Journal of Medical Sciences, May, 1922, No. 5, summarizes the results as follows:

There were 2305 girl pupils included in the tabulation of those not taking treatment and 2190 in the tabulation of those taking treatment. All were examined every six months and very careful records maintained. They divided their findings into three groups: First, those girls who had normal thyroids. Of these there were 906 in the group taking treatment and 910 in the group not taking treatment. In the group taking treatment only 2 or 0.2 of one per cent developed goiter; whereas in the group not taking treatment 347 of the 910 developed definite enlargement of the thyroid, or 27.6 per cent.

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[19] See bibliography.

Of those with a slightly enlarged thyroid, there were 477 in the group taking treatment, of which only 3 were recorded as having the goiter increased; whereas, in those not taking the treatment, there were 127, or 13.3 per cent where the goiter was increased. Similarly, of those with slightly enlarged thyroids, 659 of those taking treatment were recorded as having a decrease in the size of the goiter, whereas in those not taking treatment only 134, or 13.9 per cent, showed decrease.

In the group with moderately enlarged thyroids, of those taking treatment there were 29, or 20.3 per cent, showing no change; and of those not taking the treatment, 57, or 64 per cent. Of those taking treatment none were recorded as having an increase in the size of the thyroid, where it had been recorded as moderately enlarged to begin with, while in those not taking treatment 21 of this classification showed enlargements, or 23.6 per cent. But even more striking is the evidence of therapeutic effect; for in this group with moderately enlarged thyroids of those taking treatment 114, or 79.7 per cent, showed a decrease. There is, therefore, strong evidence that the administration of the iodin had both a very marked prophylactic and therapeutic effect.

Since the publication of this practical test developed by Marine and Lenhart in their intensive researches, the procedure has been carried out in a great many countries as well as many districts of this country, and practically always with the same most gratifying results. With regard to the possible ill effects Kimball reports that, in all the cases taking the prescribed two grains of sodium iodide twice yearly, there was not a single evidence of exophthalmic goiter nor any evidence of a nervous irritability simulating it; and in all the cases only 11 of iodide rash, 6 of which were so mild as not even to require treatment. Less than one-half of one per cent showed any lesion or evidence of disturbance from the treatment. The importance of this cannot be overestimated since in many districts, such as the glacial areas of Switzerland, Alaska, and British Columbia, a very large percentage of the humans and animals suffer from endemic goiter, and both are equally easily controlled, results being practically complete; and goiter is now considered one of the easiest of the known diseases to prevent.

The result of this practical test of the value of new facts brought out by laboratory experimentation has been that the children in many inland communities in America and all children in Switzerland are compelled by law to be given the iodin at regular periods. If space permitted, it would be of interest to refer to other phases of the role of iodin in thyroid functioning and general metabolism. Two others will be sufficient.

Animals are often involved as are humans. In a district of British Columbia where the iodin is particularly scarce in the soil and therefore in the plants and foods, it was found impossible to raise hogs because the young had little or no hair, had rough scrofulous skin, and failed to develop properly. The administration of a few grains of iodin to the pregnant sows, completely corrected the condition, so that now the raising of hogs in that district is carried on with as great ease and perfection as in normal communities. The humans in this district were also seriously affected.

Similarly, the fish in a hatchery of a neighboring state were dying off at such a rapid rate, that it seemed necessary to abandon the entire enterprise. At the suggestion of Dr. Marine who found on examination that these fish were suffering from goiters, they were given iodin in their food. This completely cured the malady.

It is a very frequent experience to find acute thyroid involvements subside rapidly and often apparently completely with removal of dental infections. In Chapter 60 I have discussed in detail such a case. It is of particular interest first because the systemic symptoms cleared up very completely and the local thyroid enlargement reduced approximately to normal. Two years later with the development of an apical involvement of another tooth, the symptoms returned similarly, and if possible, more severely than at first, since there was a very considerable heart involvement, as tachycardia; and after the removal of this infected tooth the symptoms and the activity of the thyroid both disappeared. This condition of disfunction of the thyroid is so frequently met in our clinical work, that we look upon it as one of the very common systemic expressions of dental infections.

In the above chapter I refer to several cases with a discussion of the clinical phases, which illustrate clearly, without repetition here, that the removal of the dental infections in a large number of these cases completely relieves the acute disturbance, and the thyroids return to an approximately normal functioning, and otherwise very grave symptoms disappear. In that chapter on Endocrines I also discuss the thymus and parathyroids.

In further study of the improvement in functioning of glands of internal secretion by removal of dental infection, I will discuss the effects of dental infections on ovaries and testicles. A causative factor frequently associated with infections of these glands is an infective process which, because of the nature of the tissues involved, induces individuals suffering from such disturbances, to suffer in silence, notwithstanding their knowledge that there has been no opportunity for such an infection. In the chapter on Primary and Secondary Sex Organs I recite the details of a number of cases where the evidence seemed very strong that the dental infections were the primary factor in involvement of these tissues. A brief review of some of these is as follows:

A uterine discharge thought to be malignant in origin, which had persisted for six months and was growing progressively worse, entirely disappeared and has not returned for two years by the removal of dental infections, illustrated in a figure of Chapter 62. A young woman, typical of many, suffering from a very severe suppression at the time of her periods, accompanied by marked mental disturbance, was completely relieved by the removal of dental infections. The condition, however, returned, and the removal of further dental infection completely corrected the trouble without return for a year and a half. A man with a painful swelling of the testicles had the condition greatly relieved by the removal of dental infections. All of these cases are further discussed in succeeding paragraphs under the heading of the Production of the Disturbances in Animals by the Inoculation of Dental Infections from Involved Patients.

While it has been known for some time that the pancreas plays a very important role in the metabolism of carbohydrates, the proof that the Islets of Langerhans furnished an internal secretion capable of correcting this disturbance, has not been available until the epical work of Banting, Best, Macleod, etc., through the isolation of insulin. When this substance is injected into normal animals, there is an immediate reduction of the blood sugar; and, similarly, when injected into animals from which the pancreas has been removed and which have thereby been induced to develop typical diabetes, the blood sugar is reduced in accordance with the dose of insulin injected. While it has been known that the pancreas plays this important role in the development of diabetes, it is not known what factors have been most active in causing this disturbance of the pancreas.

In the course of these researches on The Relation of Dental Infections to Systemic Disturbances, many important new facts have been developed through the study of the chemical changes in the blood. Among these the changes in the blood sugar, due to the removal of dental infections, has been a very important one. A group of these cases is shown in Figure 131 of Chapter 20.

A first effect of the disturbance of dental infections in cases of hyperglycemia is an aggravation of disturbance regardless of the method of conducting the surgery. These patients are poor risks for surgical operations, whether in the mouth or elsewhere. In another chapter I speak of the serious effect on these patients of the use of adrenalin. Since adrenalin is capable of producing in individuals or in animals an increase in blood sugar, or a lowering of the rate of metabolizing of carbohydrates, its injection with the anaesthetic, as is common practice with novocain to produce a more prolonged anaesthesia, frequently causes a very sharp rise in blood sugar in patients already suffering from a mild hyperglycemia, and an alarming rise in patients with a severe sugar retention. It is, of course, obvious that in these patients the use of adrenalin must either be entirely dispensed with or reduced to a minimum.

In ordinary dental practice diabetics are frequently presenting for service, who do not themselves suspect such a condition; and except he be trained in the methods of diagnosis, the dentist will rarely suspect the condition unless the patient has informed him. In our clinic where we make very frequent chemical analyses of the blood as part of our research, we find a large number of patients with a mild or even severe diabetes mellitus who have no suspicion of the condition. Nor is an analysis sufficient for establishing the presence of a diabetes mellitus, since there may be either an abnormal condition of the kidney, which allows sugar to pass from the urine into the blood even though the blood sugar is not up to the threshold of danger, or the sugar may be above the threshold in the blood, and not be present as a glycosuria. We do not consider that the reduction in blood sugar is of itself sufficient evidence to justify the conclusion, that the pancreas has been injured by the presence of dental infections, even though carbohydrate metabolism is definitely improved by the removal of dental infections. We would, accordingly, wish to consider the data in this paragraph in connection with that in the next section on the effects on animals.

II. THE PRODUCTION OF DISTURBANCES IN THE GLANDS OF INTERNAL SECRETION OF ANIMALS BY THE INJECTION INTO THEIR CIRCULATION OF CULTURES TAKEN FROM TEETH OF INVOLVED PATIENTS.

It is very significant that in the inoculation of over 1500 rabbits with cultures from dental sources taken from patients suffering from various disturbances, it is exceedingly rare that the glands of internal secretion are directly invaded by organisms, unless the patient from whom the dental infection was taken was suffering from an active process. This does not mean that all animals inoculated become so infected; nor does it mean that this becomes of necessity a competent method for diagnosing whether or not the patient has such an involvement. In the chapter on Elective Localization of Organisms, I have showed that the quality of elective localization is directly related to the culture medium furnished by the patient, and that a patient, with a diseased organ tends to furnish a modified culture medium, which in many instances seems to develop in the organism an elective localization for that tissue. We are not able to determine the completeness of the vicious cycle: namely, the role of the organ, furnishing to an individual with a disturbed general defense, a toxin and bacterium which attacks the involved tissue already injured by some other cause, which diseased tissue furnishes some substance to the blood stream which develops or seems to induce in the organisms an affinity for that particular tissue. That this quality is transient in the organisms we have showed by the fact that, when they are grown on artificial media for a short time they tend, usually, to lose this elective localization quality; but that it is specific to a degree in the organism during the immediate period following its transfer from the dental infection of the patient suffering from that lesion, to an animal without a lesion in the similar tissue, where it tends to develop disturbances in normal tissue of the type of that which is diseased in, or invaded by, infection from the dental infection of the patient.

To save repetition of illustrations we do not present here many of the reproductions of these lesions in animals, of which a large number of cases are shown in the chapters on Primary and Secondary Sex Organs and Endocrine System. Briefly these results show as follows: In the case shown in Figure 148, Chapter 22, four female rabbits were inoculated with the culture taken from the teeth of a girl suffering from acute ovarian involvement, and all four developed infection of the ovaries and tubes, or 100 per cent; whereas, in the total number of fifteen hundred rabbits inoculated, of which approximately half are females, this involvement has not been recorded in one per cent of the females. In the case referred to under the previous heading with purulent uterine discharge one of the rabbits inoculated developed an acute infection of the ovaries, tubes, and uterus. In the case shown, illustrating the patient suffering from pain and swelling of the testicles, three rabbits were inoculated with cultures from three different teeth. All three developed, as shown in illustration of same in Part Two, acute infection of the testicles; whereas, in approximately 750 male animals inoculated with cultures taken from dental sources, not one per cent has shown involvement of these tissues.

A typical illustration is shown in a figure of Chapter 62 in which case the patient had suffered from an ovarian cyst which was removed eight months previously and was approximately the size of a goose egg. Five female rabbits were inoculated with the culture from her extracted tooth and two developed cysts of the ovaries. Two of these are shown in Figure 191. One has three small cysts on each ovary. The rabbit was posted too soon to permit them to grow very large. Large ones produced in rabbits are shown in the chapter on Primary and Secondary Sex Organs.

In the previous section of this chapter we have referred to the role of dental infections in relation to the pancreas, and diabetes as seen in the clinical study of these cases. We have tried experimentally to produce typical diabetes by the inoculation into rabbits of cultures from the teeth of patients suffering from acute diabetes. The blood sugar of this patient was 130 mgs. per 100 cc. After the removal of her dental infections, she had a very sharp reaction which put her to bed for a few days. The culture grown from her tooth increased the blood sugar of the rabbit from 97 to 149 with a single injection of the strain. A reinoculation of the rabbit with this strain again produced a rise in the blood sugar. Figure 192 shows the normal histology of the pancreas of a rabbit. Figure 193 shows the pathological histology of the pancreas of a rabbit in which an artificial diabetes has been produced. A pathological pancreas has a decreased number of functioning Islets of Langerhans, which is a very difficult condition to reveal histologically.

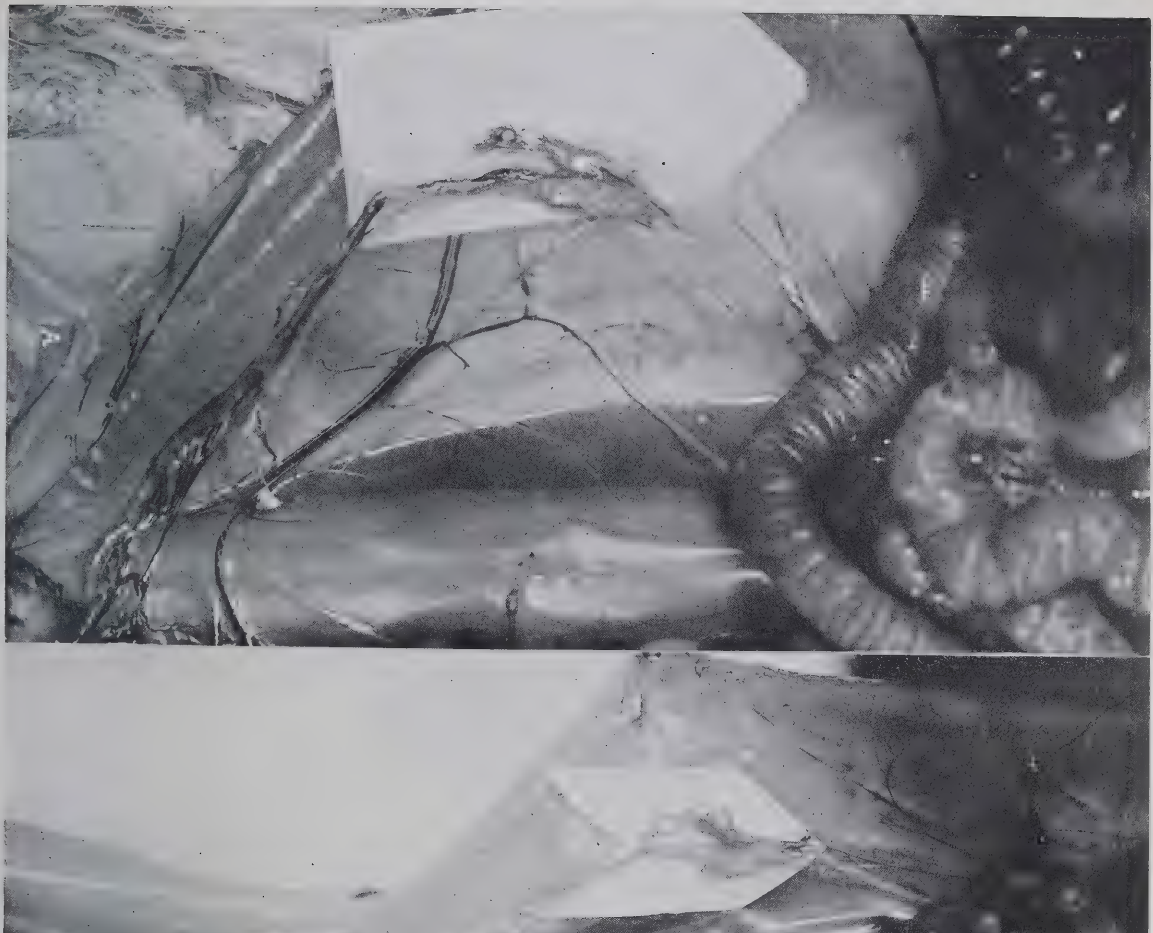
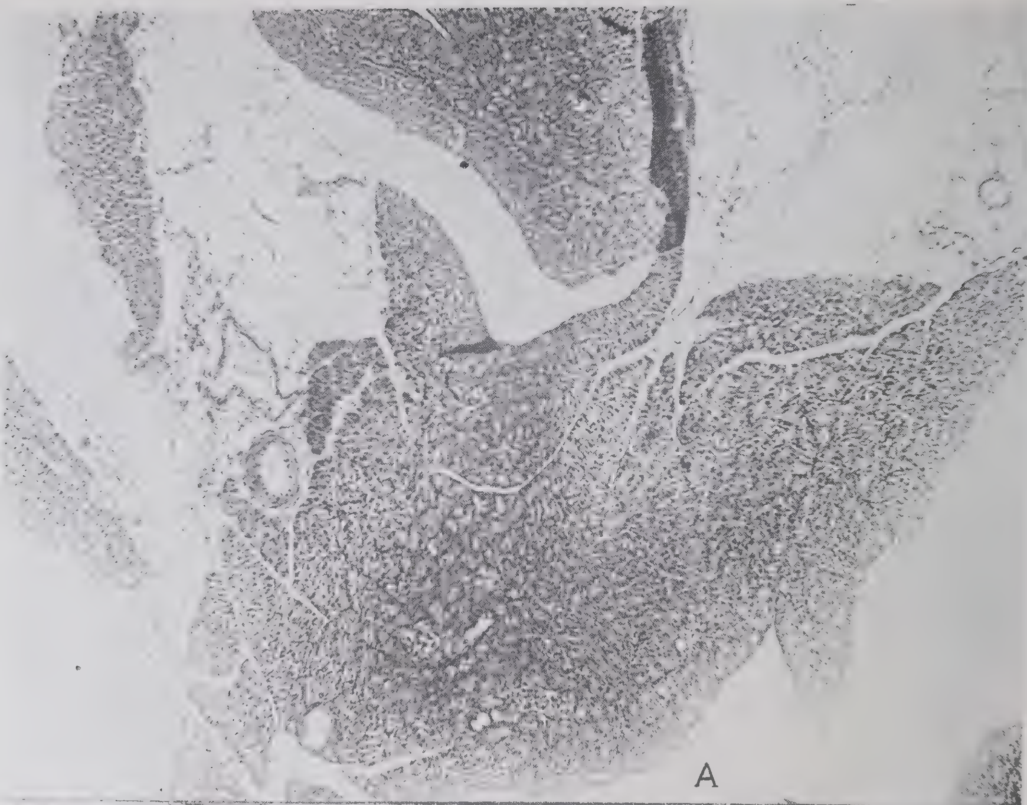


FIGURE 191. TWO RABBITS WHICH DEVELOPED OVARIAN CYSTS. PATIENT FURNISHING CULTURE HAD RECENTLY BEEN OPERATED FOR SAME.



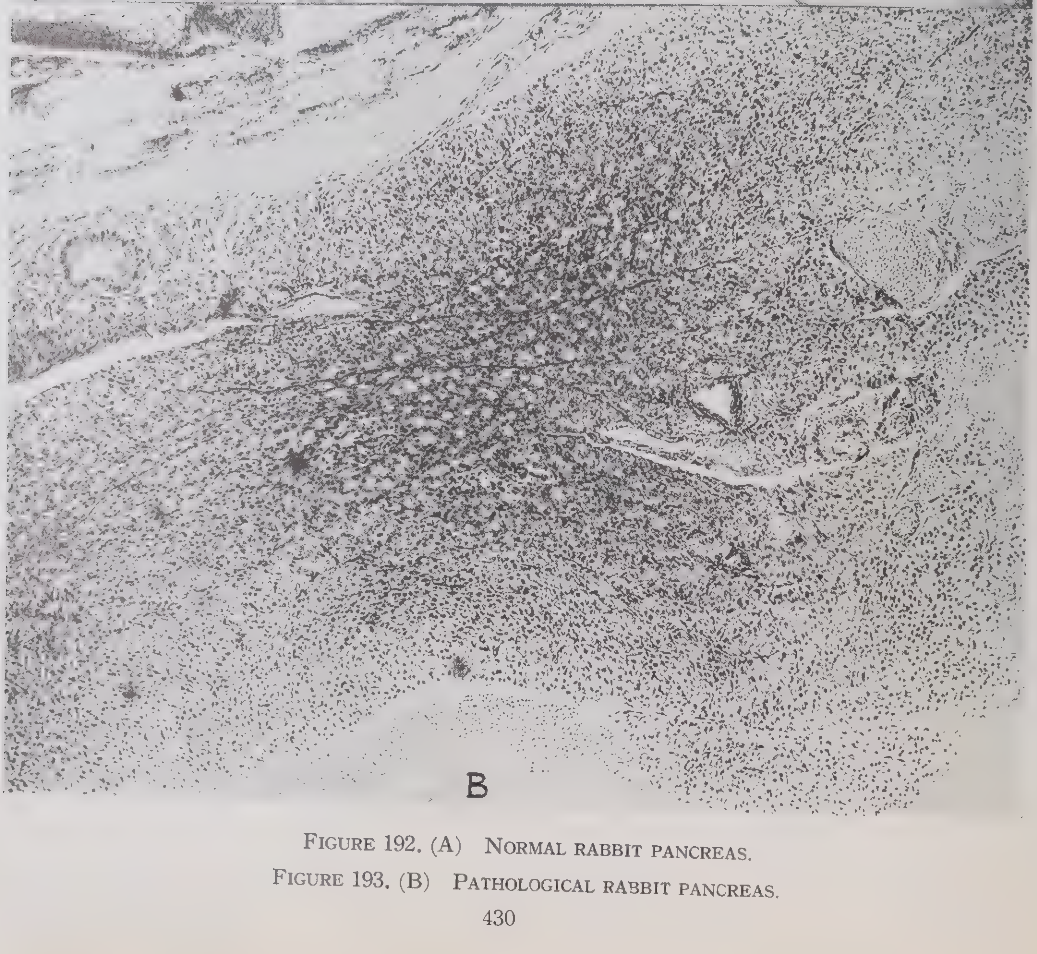


Figure 192. (A) Normal rabbit pancreas.

Figure 193. (B) Pathological rabbit pancreas.

The only interpretation we are able to make of these phenomena is that dental infections tend under certain conditions to involve the glands of internal secretions in the animals inoculated when these cultures are taken from patients suffering from acute involvements of these tissues.

III. THE MODIFICATION OF THE PATIENTS' SYSTEMIC INVOLVEMENTS PRODUCED BY DENTAL INFECTIONS BY THE ADMINISTRATION OF EXTRACTS OF THESE GLANDS.

One of our most difficult problems has been to ascertain the role of the glands of internal secretion in the presence or absence of a defense against dental infections. Relatively little is known as to what constitutes the chief elements in the mechanisms of defense. Some elements, however, seem pretty definitely established or at least strongly suggested. Since patients with a good defense have, as a group, a high ionic calcium of the blood in contrast with a relatively lower ionic calcium of the blood in patients with a low or broken defense, we seem justified in concluding that in some way this element, whatever the factors are which it may represent, is indicative of the nature of the defensive mechanism of the patient. In the preceding chapters I have brought out the following important facts:

With the elimination of dental infections there tends to be a marked rise in the ionic calcium of the blood, when it is depressed, with a reduction of the pathologically combined calcium of the blood, if we are correct in our interpretation of our data. In some cases, in spite of the elimination of dental infection, the patients remain on a low level, as though they fail to have the mechanism functioning which should bring about the reëstablishment of a normal defense and normal functioning. These cases are very slow to recover. In their case the prognosis is bad. They tend continually to recurrence and tend, in general, to have an unfavorable prognosis. We have endeavored to whip up the defense in these cases by various means such as autogenous vaccines and with very definite betterment in many instances. In some cases, however, in spite of the removal of the dental infections and the effort to whip up the defense with a vaccine, the results, as judged by the clinical improvement, have been very limited. This failure to improve physically has been paralleled by a failure of the ionic calcium to be improved toward normal. This has strongly suggested the absence of some activating substance which either combines with the toxic substance of the involved infections, or which reinforces the patient's defensive mechanism.

In the chapter on Serological Studies we have showed the suggested relationship of the ionic calcium to the activity or normal functioning of the cells of the body. With an increase of the calcium beyond the normal, sugar readily passes from the blood, through the kidney, with the urine. We have tried the injection of ionic calcium in both rabbits and patients in such diminutions and quantities, as would make the absorption of the calcium readily possible, with limited success, as indicated by the raising of the ionic calcium of the blood. In some cases there would be a prompt improvement, which advantage would be lost, also, quite promptly.

In thyroidectomized dogs it was early found that there was a tendency to development of tetany. It was later shown, however, that this was due not to the removal of the thyroid but the removal of the parathyroids, for the animals from which the thyroid was removed, without the removal of the parathyroid, could be kept alive by the administration of thyroid extract, but would die if the thyroid extract were not administered; and, similarly, the removal of the parathyroids, without the removal of the thyroid, produced a tetany and death which, however, could be prevented by the planting in the animals' tissues of parathyroid tissue. In either case the animals lived if a small quantity of both thyroid and parathyroid tissue was left. It was also shown that the removal of the parathyroids was accompanied by a depression of the ionic calcium of the blood, and that the injection of ionic calcium into the blood stream of an animal developing this tetany, relieved the symptoms. This has strongly suggested that the parathyroids are very directly related to the metabolism of calcium.

I have, accordingly, endeavored to raise the ionic calcium of the blood by the administration of parathyroid extract to patients suffering from dental infections, from which they did not readily recover, after the removal of the dental foci. Such a case is the following:

Case No. 1267.—A man, fifty-seven years of age, presented with the following history. His mouth was closed by swelling, which developed some months after the extraction of a mandibular molar tooth of the same side, some months previously. This operation had been made under gas, which excluded the possibility of the local anaesthetic's having lowered the defense, locally, of the tissue, or of infection having been carried in with the hypodermic needle. It was exceedingly difficult to make a physical examination, due to the muscle spasm and the patient's prostration. He was so physically weak, that he had to be helped and almost carried into the ward. Pus was located and drained from the internal border of the ramus distal to the position from which the tooth had been removed, and no infection had developed through the socket which had healed. This man had other dental infections which were removed, and the sockets healed slowly, but completely. There was a continual recurrence of the disturbance of the tissues about the left angle of the mandible, with a final cellulitis and lymph adenitis. Two enlarged lymph glands were opened surgically by his surgeon; by the maintenance of packs in these incisions, drainage was maintained, which wounds, if permitted to close, caused him immediate return of more acute symptoms. This involvement of his neck seemed quite distinctly separated from any possible zone of necrosis of the mandible.

The ionic calcium of his blood, which would normally be about 10 to 10.5 mgs. per 100 cc., stood at 7.5; and the use of tonics and the removal of dental infections failed to bring it up appreciably, suggesting an unfavorable termination, as the case was progressively getting worse. The clinical picture was complicated by a history of previous positive Wassermans. Parathyroid extract, one-tenth of a grain per day, was administered by me to determine its effect in increasing the ionic calcium of the blood, as well as upon his general clinical condition. In addition to the administration of the parathyroid I placed him on a diet, intended to increase, as rapidly as possible, his ionic calcium: namely, two quarts of milk a day, or preferably the same quantity of buttermilk, and two or four tablets of calcium lactate with each meal. Promptly the ionic calcium of the blood began to rise, increasing about 1 mg. per month per 100 cc.; and with this improvement in ionic calcium, his physical condition improved; the flowing fistulæ in his neck and extensive induration subsided and completely disappeared; his general physical condition returned rapidly to normal, so that in five weeks' time he gained six pounds in weight, which was more improvement than is indicated by the weight, since a part of his previous weight was edema. He was able to take up his work in a few weeks' time, increasing his hours rapidly, and in approximately eight weeks was carrying his original heavy load with several extras; and in twelve weeks, according to one of his associates, was doing much more than an ordinary man's capacity of the hardest kind of mental and physical work.

EFFECT OF PARATHYROID AND CALCIUM LACTATE TREATMENT ON IONIC CALCIUM OF BLOOD

Date	Hour A. M.	Treatment for Ionic Calcium	Ionic Normal Serum	Ionic Treated Serum	Combined Patho-logical
8-31-22	9:00	Began	7.5	9.7	2.2
9- 6-22	10:00	Continued	7.9	9.9	1.9
9-13-22	11:00	Continued	8.1	9.5	1.4
9-26-22	11:00	Continued	8.2	9.4	1.2
1-24-23	11:00	Discontinued	10.6	11.0	0.1
2-16-23		Resumed	9.2	11.1	1.8
4-25-23		Continued	9.4	9.9	0.5

FIGURE 194.

The progressive changes in this case are shown in the table in Figure 194.

Another striking case is as follows: A young mother, who had had a miscarriage soon after the birth of her previous child, was suffering from rheumatism, probably related to dental infection. The ionic calcium of her blood was 8.2. In two weeks' time after the removal of her dental infection and with the assistance of parathyroid and calcium lactate, her ionic calcium had increased to 10.4, her rheumatism had disappeared, and instead of being discouraged and despondent, she had regained her normal state of vivacity, hopefulness, and pleasure in life.

But all cases do not respond thus readily to the administration of parathyroid. In contrast with the above, I will cite the following: This patient had multiple deforming arthritis. His ionic calcium was reduced to 7 milligrams, with 3 milligrams pathologically combined. He was placed on a special diet of milk, calcium lactate, and a general mixed ration plus parathyroid. His condition improved but slightly, though definitely, but tended rapidly to settle back to his former condition. Removal of his dental infections did not materially improve his general condition which had existed for several years. The administration of parathyroid and calcium lactate only increased his ionic calcium from 1½ to 2 milligrams. There was evidence that he was suffering from some other source of toxic involvement, that was so extensive, as to keep him continually overwhelmed. He was referred to specialists for the study of his digestive tract; and after being placed on a rigid rest treatment combined with hydrotherapy, he became more comfortable but with only slight improvement. They found a chronic colitis, which it seemed probable accounted for these symptoms and general reactions. The patient had felt definite improvement from the milk diet and requested that he be placed on that exclusively, of which he took four quarts daily. The result was that he experienced a marked improvement in the arthritic disturbances, and his ionic calcium coincidentally increased about four milligrams. We interpret these results as follows:

On the milk diet, there was a distinct change produced in the bacterial flora of the entire intestinal tract, particularly of the colon, coincidentally, a change in the acid-base balance of the fluids of that tract. The toxic substances to which he had become sensitized and which were produced in that tract were reduced because of the reduction of the flora that had generated them. With the elimination of this toxic source, his blood was able to maintain its ionic calcium which otherwise was neutralized by this toxic substance, besides which there was undoubtedly a distinct beneficial effect upon this local tissue from the presence of the milk products. The increased ionic calcium of the blood would rapidly raise the defense and repairing power of the diseased tissues of the colon; and just as the vicious cycle had tended to get worse and worse previously, similarly, by the increase in ionic calcium of his blood, the repairing power of the local tissue increased and the absorption of toxins decreased, the significance of which seems to be, that the administration of parathyroid and the forced intake of a calcium furnishing diet will be of no avail in a system suffering severely from the presence of a toxic generation and absorption of the same or similar type as that in a dental focus with which we are concerned; and this explains probably in large part why the removal of the dental infection produces in many cases either a temporary or a limited beneficial effect.

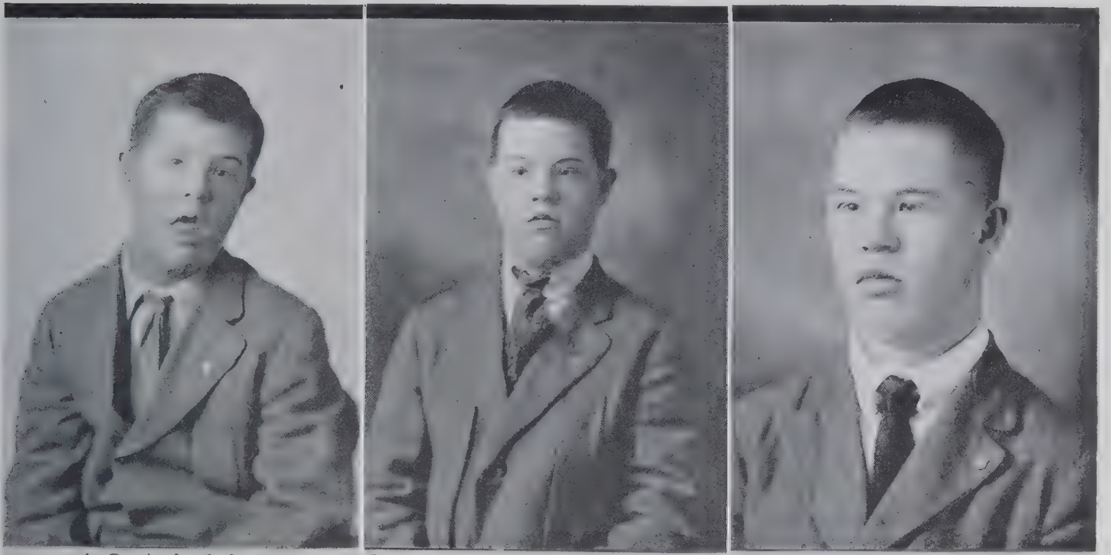
IV. THE IMPROVEMENT OF THE FUNCTIONING OF THE GLANDS OF INTERNAL SECRETION BY THE MECHANICAL STIMULATION INDUCED BY THE MOVEMENT OF THE BONES OF THE FACE AND BASE OF THE SKULL.

One of my earliest experiences, in this connection, was with a case which showed conspicuously the interrelationship between the pituitary and the development of the bones of the face. This boy at the age of sixteen was infantile in many of his characteristics and developments. The genitals were those of a boy eight years old. The facial expression was that of the typical Mongolian idiot. By the Binet test he had a mentality of about four years. Roentgenograms of his hands showed that the epiphyseal bones had not united. He played on the floor with blocks and with rattles like a child. His interest was in children's activities.

The characteristic physical condition was that his maxillary arch was so much smaller than the mandibular arch that it went entirely inside it. In order to give him a masticating surface and with the hope of helping him both physically and mentally, since I had had several cases greatly benefited by such an operation, I determined to widen his arch by moving the maxillary bones apart about one-half inch. The position of his teeth before is shown in Figure 195-D. Roentgenograms showing the opening of the median suture with increase of pressure are shown in Figure 196.

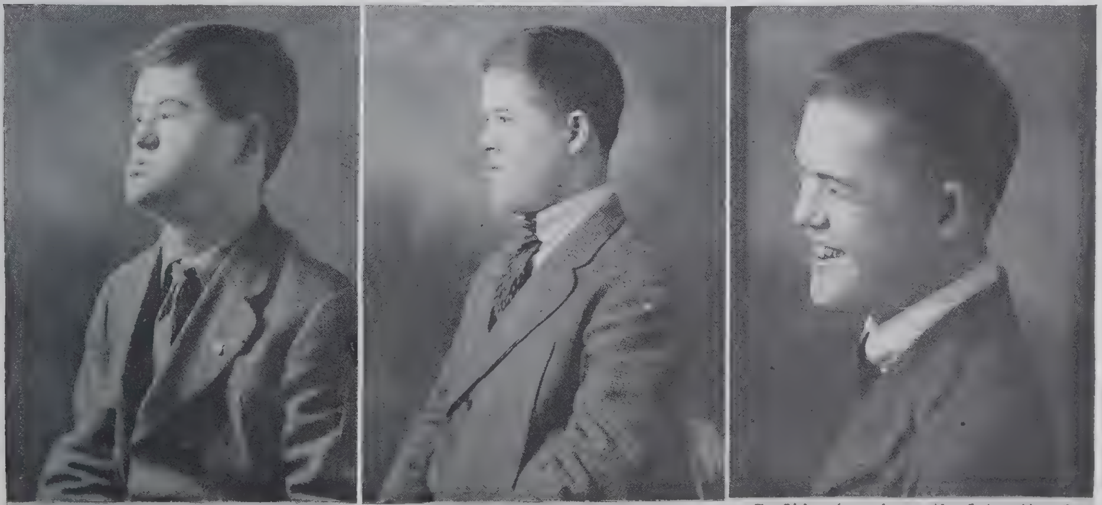
An important phase of this case was that the left nostril was entirely occluded and had been probably all his life. A rhinologist spent a half hour trying to shrink the tissue with adrenalin and cocain sufficiently to get air or water through, and was not able to do so. He was able to breath only through his mouth. The quantity of air that he was able to secure through his right nostril was so scant that he continually breathed with his mouth open. At night he was forced to lie with something like his coat rolled into a ball and placed under the back of his head and his head pushed far back so that this position would open his mouth and retain it so, or he would awaken by strangling himself with the closing of his mouth.

He had the innocence and utter lack of sense of modesty of a child; would undress under any conditions before strangers. With the movement of the maxillary bones laterally, as shown progressively in Figure 196, there was a very great change in his physical development and mentality. He grew three inches in about four months. His moustache immediately started to grow; and in twelve weeks' time the genitals developed from those of a child to those of a man. His mentality change was even more marked, as the median space between the maxillary bones was widened to one-half inch in about thirty days, and by some process which I have interpreted as probably being a prying down of the base of the skull, thereby reducing by the leverage of the



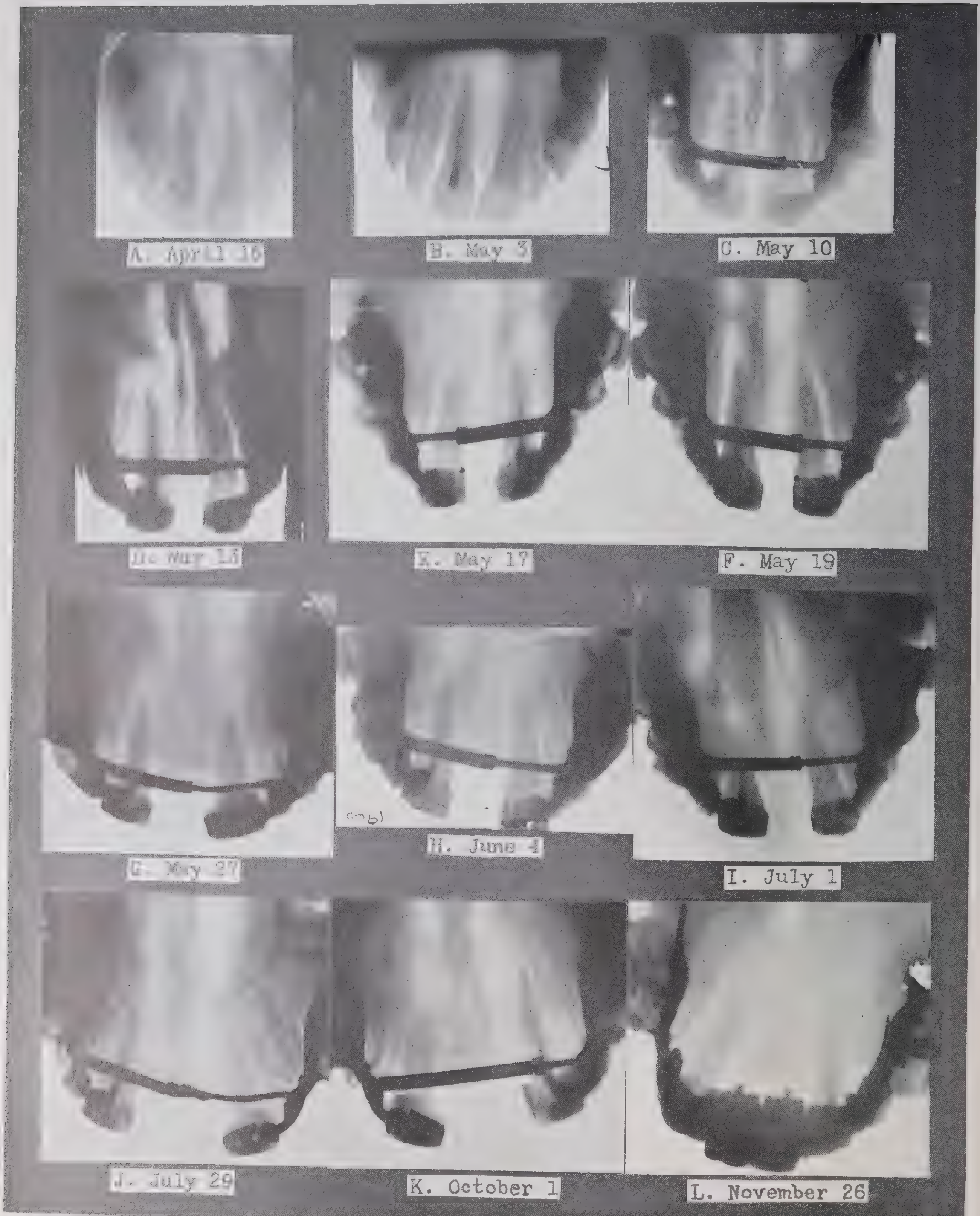
A. Front view before. B. Front view thirty days later than A. C. Front view six months later than A.

Figure 195. Front view. Changes produced by slowly opening the median suture. Case No. 111. Age sixteen. In about twelve weeks he passed through the changes of adolescence, rapidly growing a mustache, etc.



D. Side view before. E. Side view thirty days later than D. F. Side view six months later than D.

Figure 195. Side view. Changes produced by slowly opening the median suture. Case No. 111. Age sixteen. The mental changes were also very great. He passed from playing with blocks to the interests of developing boyhood, telephoning, reading, etc.



A. April 16
B. May 3
C. May 10
D. May 15
E. May 17
F. May 19
G. May 27
H. June 4
I. July 1
J. July 29
K. October 1
L. November 26

Figure 196. Roentgenographic changes by days from opening the median suture.

maxillary bones on the temporal bones, a pressure upon the hypophysis cerebri or pituitary in the sella turcica, and thereby markedly changing its function. In a few weeks' time he passed through stages that usually take several years; at first, getting behind the door to frighten us, later, putting bent pins on chairs to see us jump when we would sit down, and finally being the cause of a policeman's coming into the office from where he was conducting traffic on the corner below to find who it was squirting water on him when his back was turned. He developed a great fondness for calling people over the telephone, wanted to borrow my automobile to take his mother for a drive, and with his arm caressingly about the shoulders of one of the secretaries invited her to go with him to Euclid Beach for a dance. All this change developed in about twelve weeks' time.

A most remarkable event happened in connection with this procedure. He lived in another city, and so, while with me was kept in a boarding house at a little distance from my office in order for frequent and necessarily constant attention. On his return to his home town with the appliance to maintain the separation in place, his efficiency had increased to such an extent that his mother would send him with the money to the grocery store with the order for the day's groceries, and he could invariably bring back the right change and could tell when it was correct. He could also come to me that ninety miles by railroad and make two changes of trains and the various transfers on the street cars of the city with all the exactness of a normal adult.

But this appliance became dislodged; the maxillary bones settled together; immediately, or in a day or two, he lapsed into his old condition of lethargy accompanied by an old trouble, which had frequently been distressing, of nausea, sometimes lasting for twenty-four hours. With the readaptation of the separating appliance and the reconstruction of the retaining appliance he returned again to his other state.

But a new problem had been developed. We had changed an infant to a potential man with all of the instincts and impulses of a man but with the mind of a child. It became necessary for his family to make changes because of the death of his mother, and the marriage of his sister, and he was accordingly placed in a state institution where he was lost in the herd, all receiving approximately the same care. During this period under which he was in my care he had learned to read and spent much time doing so.

Figure 195 shows his appearance before and after the operation, there being only thirty days' difference between each A and B, and D and E, side view. C and F show, respectively, the front and side views six months after the first picture, and it will be noted that his whiskers and moustache had started to grow. He now has the face and potentialities of a man.

In this connection I would refer to another case where a boy of eight years had less marked depression of the maxillary arch but a very marked depression mentally, such that he was not able to be taught with other children. An important characteristic of his case was that he was as timid as a bird and as dependent as an infant, was afraid of all children who might in any way cross him for fear they might hurt him, and was extremely docile to his parents. After the separation of the maxillary bones, similarly, though not so extensively, as in the latter case, his condition improved so greatly that his mother could send him to the store with the money to buy provisions and groceries and he could return with five articles which he would buy himself, and not forgetting even one. He also became the bully of the street; would come into his home boasting about how he had smashed such a big boy's nose for crossing him in something; and finally when his mother chided him for something that he did not wish to do, stating that she could not have anyone in her home who did not mind, he promptly told her that if she insisted on his doing that thing that he would leave the home. This was a complete change from his former lack of assertiveness and capacity for individual defense and responsibility. Unfortunately, domestic conditions made it necessary for this boy to be moved away from this city and for three years he was out of my care and received no attention. The final results were not so good as they should have been because of this neglect, though he never lost his assertiveness and capacity for taking responsibility.

SUMMARY AND CONCLUSIONS.

We would summarize these studies as follows:

(1) Disfunctions of various of the glands of internal secretion are often very materially corrected, and sometimes completely so, by the removal of dental focal infections.

(2) Involvements have frequently been produced

in similar endocrine tissues of the animals by inoculating them with the cultures from the teeth of the involved patients.

(3) The administration of the extracts of the glands of internal secretion, particularly of the parathyroid, is shown to be of distinct benefit in certain cases of depressed ionic calcium of the blood, due in part to dental focal infections, where this improvement has been absent or slow following the removal of the dental infections.

(4) An improvement has been produced in individuals, which we interpret to be due to a stimulation of the pituitary body, which in turn doubtless stimulates other ductless glands and together with them produces a marked change in both physical and mental states.

See bibliography references 20, 21, 22, 23, and 24.

CHAPTER XXXVIII.

THE NATURE AND FUNCTION OF THE DENTAL GRANULOMA.

PROBLEM: Is a dental granuloma a pus sac and its size a measure of the infection and danger?

EXPERIMENTAL AND DISCUSSION.

It is not without significance that the members of the laity speak of the structure which is frequently attached to an extracted root as a pus sac and something greatly to be feared and dreaded. They have very correctly reflected the thought of the professions. These researches have been undertaken to harmonize, if possible, the data that have been developed in the preceding researches here reported and the current opinion. If we were to express the public and professional evaluation of this structure it would be as follows:

Since a dental infection, if present, will produce an apical abscess, the size of that abscess will be the measure of that infection; and if it be particularly bad, it will produce a pus bag or sac which may or may not contain pus, but which is always an evidence of considerable infection.

In Chapter 3 on The Local Structural Changes Produced by Dental Infections, we found (1) that there is a large variation in the periapical structural changes that will be produced with an apparently given quantity of infected pulpal irritant, sufficient that these individuals may be graded from those having large apical involvements associated with, for example, a putrescent pulp; (2) those with this large area of apical involvement but which, instead of being diffused into the cancellous structure, is surrounded by a more or less definite zone of condensed structure, a condensing osteitis surrounds the zone of rarefying osteitis; (3) a very limited zone of destruction of apical bone with frequently a tendency to a dense bone surrounding the apical area.

In Chapter 4 we found that there is a very great difference in the susceptibility of individuals to injuries from dental infections expressing themselves as rheumatic group lesions.

In Chapter 5 we found that the individuals with the high de-

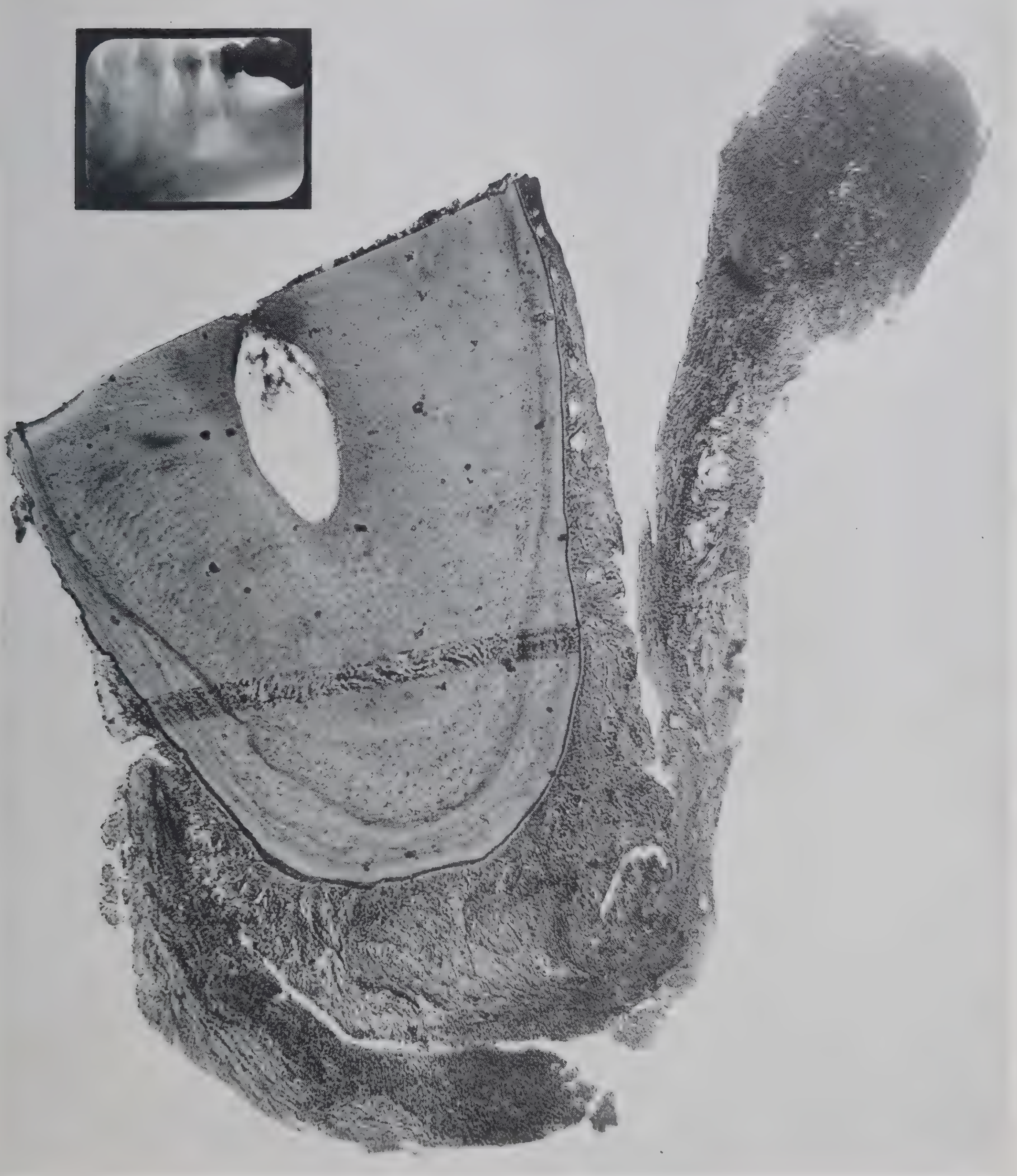


Figure 197. Appearance of a degenerating granuloma. Patient has lost her defense. Insert shows roentgenographic appearance.

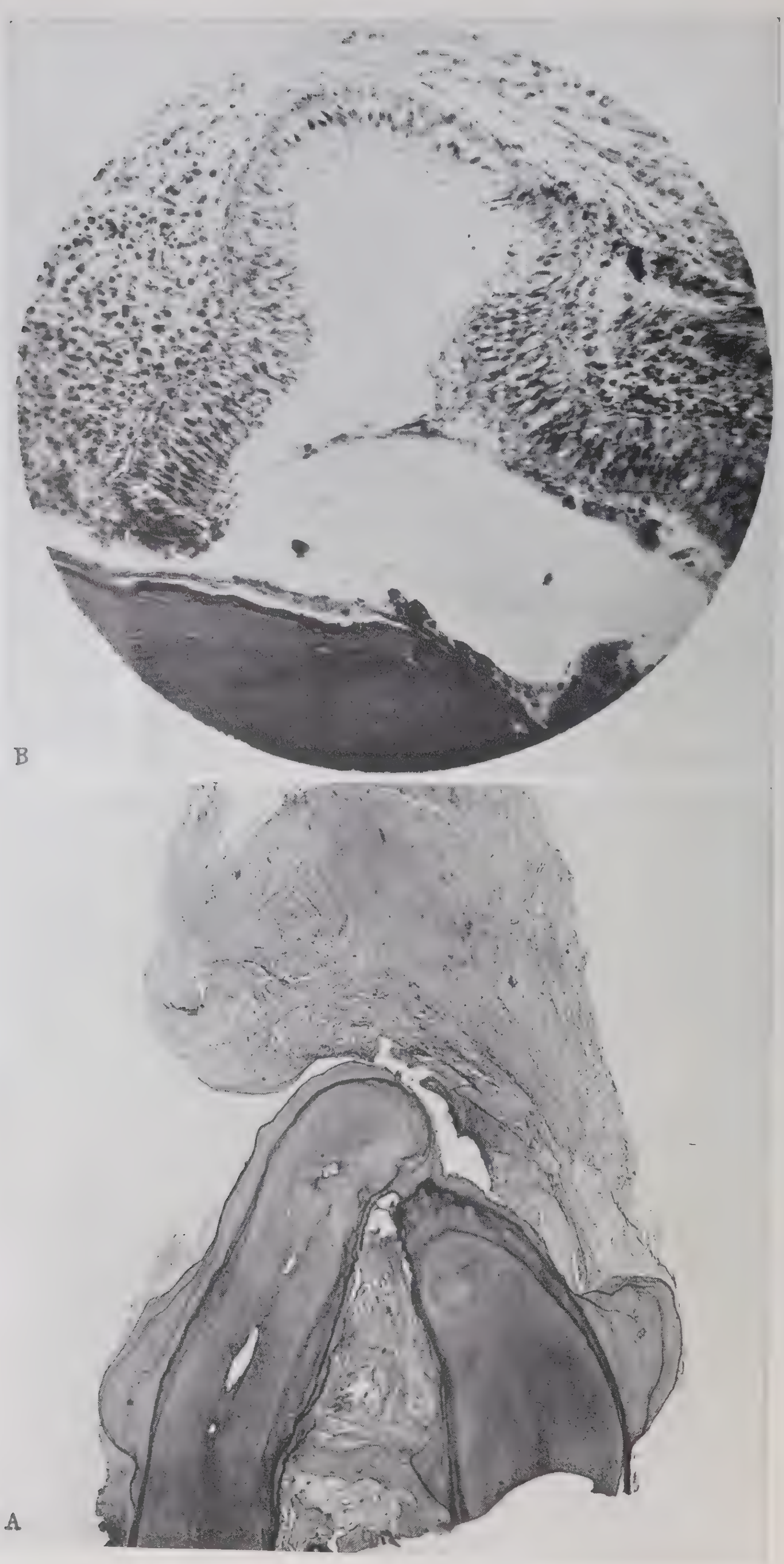


FIGURE 198. A PROTECTIVE MECHANISM OF DENTAL GRANULOMATA.

fense which protected them against injury from their dental infections (expressing themselves systemically as rheumatic group lesions) had invariably a relatively larger zone of rarefaction or bone destruction about the apex of an infected root, than did the individuals without that defense, in whom the dental infections expressed themselves readily as rheumatic group lesions; and that the individuals showing the zone of condensing osteitis surrounding the zone of rarefying osteitis generally proved to be individuals whose defense had previously been high and had been reduced, which latter we termed a state of an acquired susceptibility. This latter classification was based not on this local structural condition, but on the fact that the patient, that had previously had complete freedom from rheumatic group lesions, had suddenly acquired that condition, hence an acquired susceptibility.

Subsequent chapters revealed that dental caries tended to be much more dominant in the individuals with rheumatic susceptibility, and periodontoclasia tended to be more prominent in the individuals without the susceptibility to rheumatic group lesions.

In the chapters on serological and chemical changes in the blood and fluids of the body, the data revealed that in the individuals with a high defense, the ionic calcium of the blood tended to be high; and that it tended to be lower than normal in those with a rheumatic susceptibility; and that in the same individual, generally just in proportion as the ionic calcium returned to normal, the rheumatic group symptoms disappeared; also that these variations were produced regularly in animals by the introduction of dental infections either by inoculations or by the planting of the infected tooth beneath the skin.

These studies, and the data they revealed, strongly suggested that the tissue which developed at the root apex, and which was present in relatively larger quantities in those individuals with a high defense, was a defensive tissue placed there by Nature to establish and maintain a quarantine as close as possible to the source of infection. I, accordingly, have made a very careful study to ascertain the nature of the tissue producing this quarantine and have found a very large range in the types of tissue found at root apices. Figure 197 shows a granuloma removed with the tooth of a patient who up to six months ago had a very high defense and no rheumatic group symptoms, but during the past six months following a cold or Flu she has had quite persistent neu-

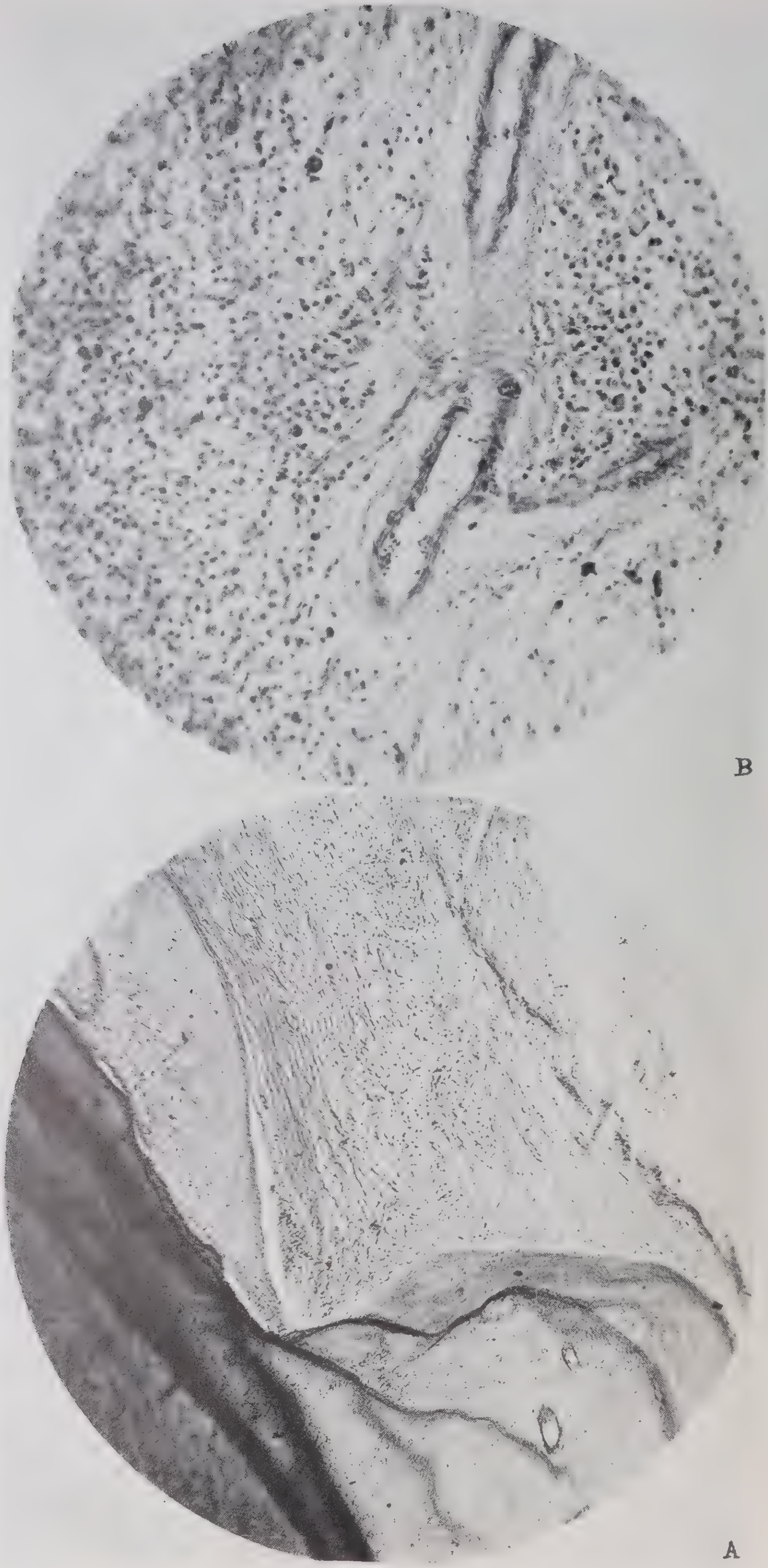


FIGURE 199. HIGHLY VASCULAR GRANULOMA OF FIGURE 198.

ritis. Note the very large lumen in this granuloma, consisting of necrotic tissue, leucocytes, and bacteria. The insert shows the roentgenogram of the tooth before extraction, and it will be noted that there is a definite zone of condensing osteitis surrounding the area of rarefaction.

In Figures 198 and 199 we see in contrast with this a granuloma which is intact, very highly vascular (shown in high power in Figure 198-B) with no necrotic and degenerated tissue, and with a very distinct epithelial membrane in contact with the root apex. These two quite divergent pathological structures are but two of a very wide range which might be inserted; and they and the structure represented in Figure 200 are presented here simply to suggest the extreme variation that may occur in these apical tissues.

In Figure 200 we see a very limited amount of fibrous capsule lying close to the denuded root end, almost entirely without vascularization, with a purulent exudate between the membrane and the tooth. I will later discuss and interpret these conditions.

If the dental granuloma is simply Nature's method of encysting a foreign substance or an irritant, it must be considered a quite different structure from that which Nature will build into a zone as the result of irritation, in which case the irritation would produce a proliferation and hence, as its name implies, a granuloma, for this is, we take it, the origin of the name that this tissue has taken. For example, Dorland's definition of a granuloma is as follows: "A tumor or neoplasm made up of granulation tissue. Dental g., a small mass of granulation tissue containing bacterial deposits on the root of a tooth." Anthony's is: "A tumor-like nodule or area of granulation tissue. Dental g., granulation tissue about the apex of a tooth usually containing bacterial deposits. Chronic inflammatory pericementitis." Ottofy's is: "A collection of leucocytes and epitheliod cells which surround the central point of irritation and resemble granulation tissue. Dental g., granulation tissue, without suppuration, at the apex of the root of a tooth or in some edentulous tissues."

Our first line of approach was to determine what Nature's reaction tends to be to mechanical irritants, in order that we might distinguish clearly between mechanical irritation and bacterial irritation. To determine this, I placed various foreign substances in the tissue under the skin of rabbits and found that if the object were sterile when inserted, Nature developed a very slight trans-

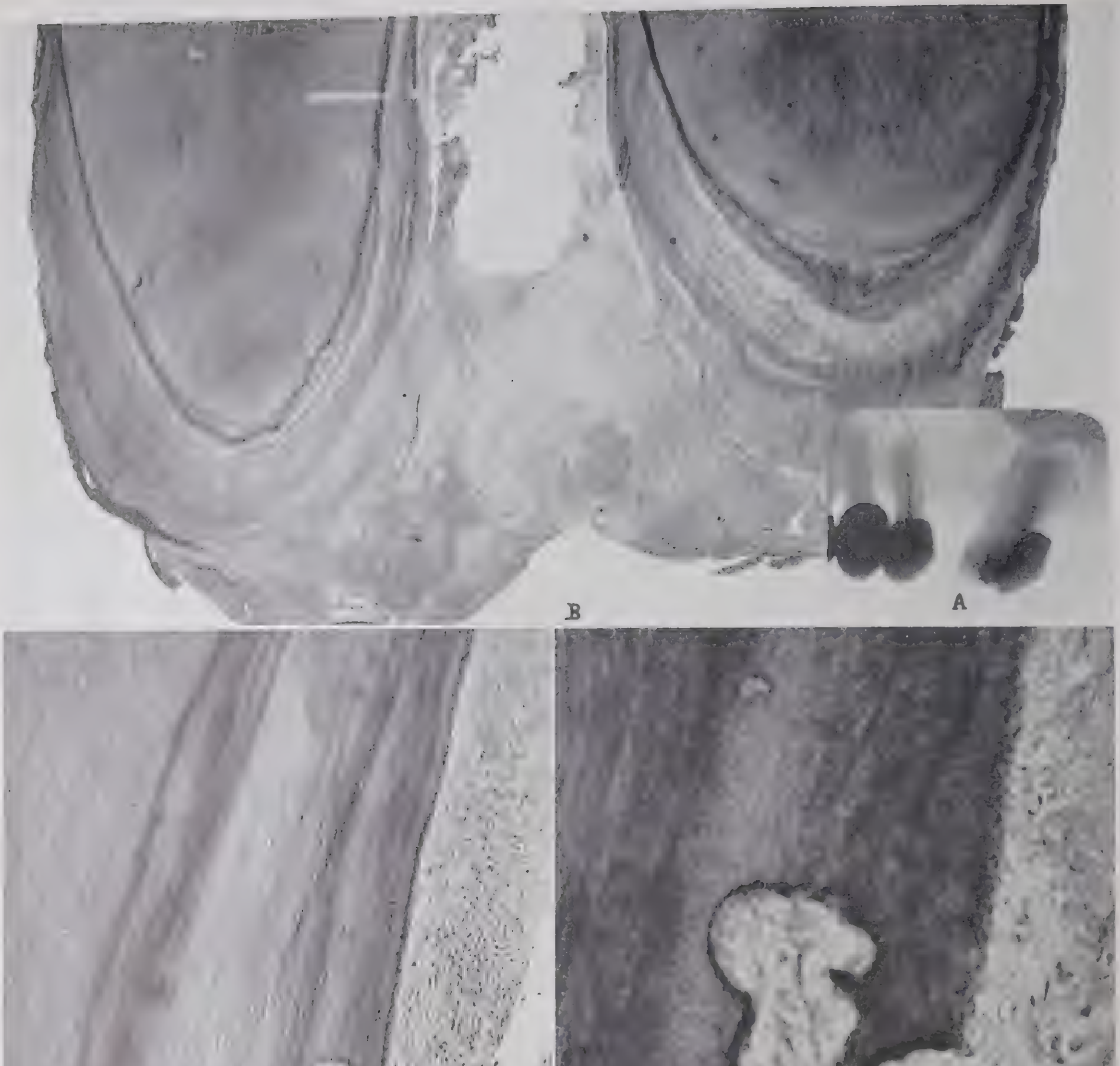


Figure 200. Resorption processes in C and D, from point of arrow in B; A, roentgenographic appearance.

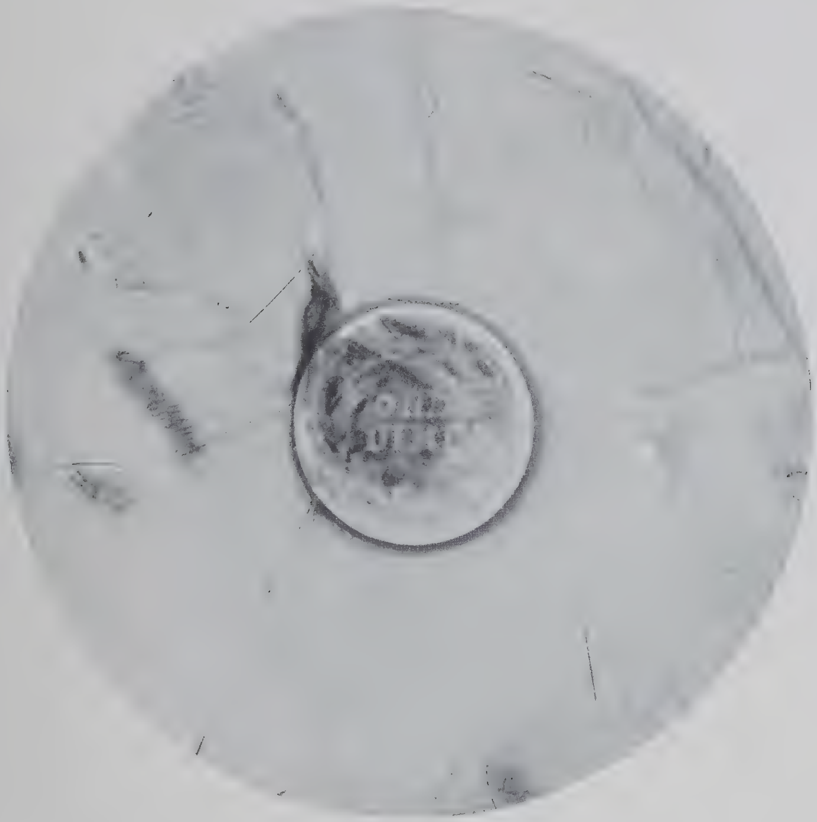


FIGURE 201. APPEARANCE OF DIME PLANTED TWO MONTHS. NOTE NO CYST FORMATION.

parent fibrous tissue about it with no tendency to proliferation or development of granulation tissue. This is well illustrated in Figure 201 which shows a dime so encysted in the tissue of a rabbit, it having been placed beneath the skin in this position two months previously. These have been left for longer and shorter periods, and the only change that is apparent is a definite evidence of etching and solution of the metal. It may be answered that this is due to the formation of albuminates with the silver and that the effect would be different with other metals. We have found little or no difference whether the foreign irritant was a piece of sterile glass or a piece of any one of the ordinary metals. It will be noted that the inscription on the dime, shown in Figure 201, can be read through the capsule as though there were no intervening tissue.

When we have placed teeth beneath the skins of rabbits or in other tissues such as the muscle, as we have now done over a hundred times in various studies, we find a very great difference in the effect. If the tooth has been free from infection, as, for example, a freshly extracted impacted third molar, there is very little more tissue built around it than around the dime shown in Figure 201. If, however, it was a pulpless tooth, with or without root filling, there is a very great difference in the reaction which it produced, ranging all the way from a closely adherent fibrous capsule entirely surrounding and enclosing the tooth, to the complete absence of a capsule, the tooth being found in a well of inflammatory exudate, sometimes with a quantity of leucocytes dead and living, and sometimes with practically no leucocytes and a pure culture of streptococci. In either of the latter cases when no capsule was formed, the rabbits were invariably killed in from a day and a half to a few weeks; and generally in less than six days. When these teeth were surrounded by a capsule they were often carried many months or a year if the rabbits were not chloroformed and posted earlier for study.

Figure 202 shows a group of encapsulated teeth that had been in the bodies of rabbits for periods of weeks or months, several of them six months. In many instances the rabbits did not show the slightest evidence of injury from these teeth. In some others, even though they were carried for weeks and had become entirely encapsulated and showed no evidence to develop local abscesses about the teeth, the rabbits developed degenerative diseases such as involvements of the heart and kidneys. Figure 203-A shows a rabbit with such a tooth placed beneath the skin, which had been taken from the mouth of a patient with nephritis. The rabbit developed acute nephritis, as evidenced by albumin in the urine, development of casts, and parenchymatous degeneration of the kidneys, as shown in B and C. In Part Two, other volume, in the study of the relation of dental infections to the degenerative diseases, I show in Chapter 63 on Nephritis a case where the same tooth placed under the skin of two different rabbits developed nephritis in two rabbits in succession, where the tooth had been taken from a patient suffering from acute nephritis.

Invariably when the rabbit built a capsule about the tooth, it proceeded to absorb the tooth; and the process is not distinguishable histologically from that process when it takes place in the mouth. Figure 204 shows a cross section of one of these fibrous capsules developed by the rabbit in comparison with the structure built about a tooth by the human; and it will be noted that, histologically, it is practically impossible to distinguish which tissue was taken from the rabbit and which from the individual. It does

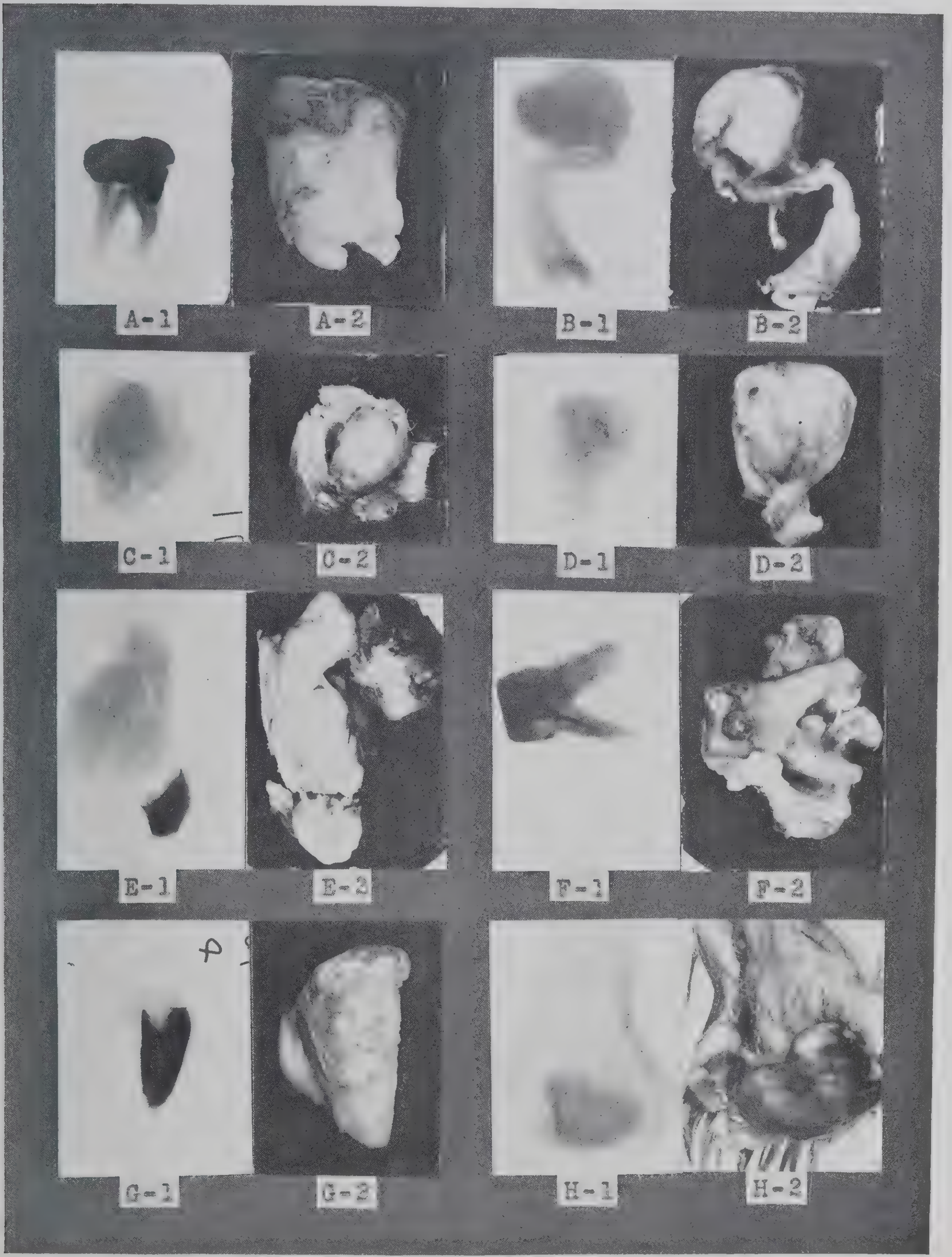


FIGURE 202. A GROUP OF ENCAPSULATIONS ABOUT IMPLANTED TEETH, PRODUCED BY THE RABBITS, AND THE ROENTGENOGRAPHIC VIEWS OF SAME. NOTE ABSORPTION OF TOOTH, B-1, C-1, D-1.

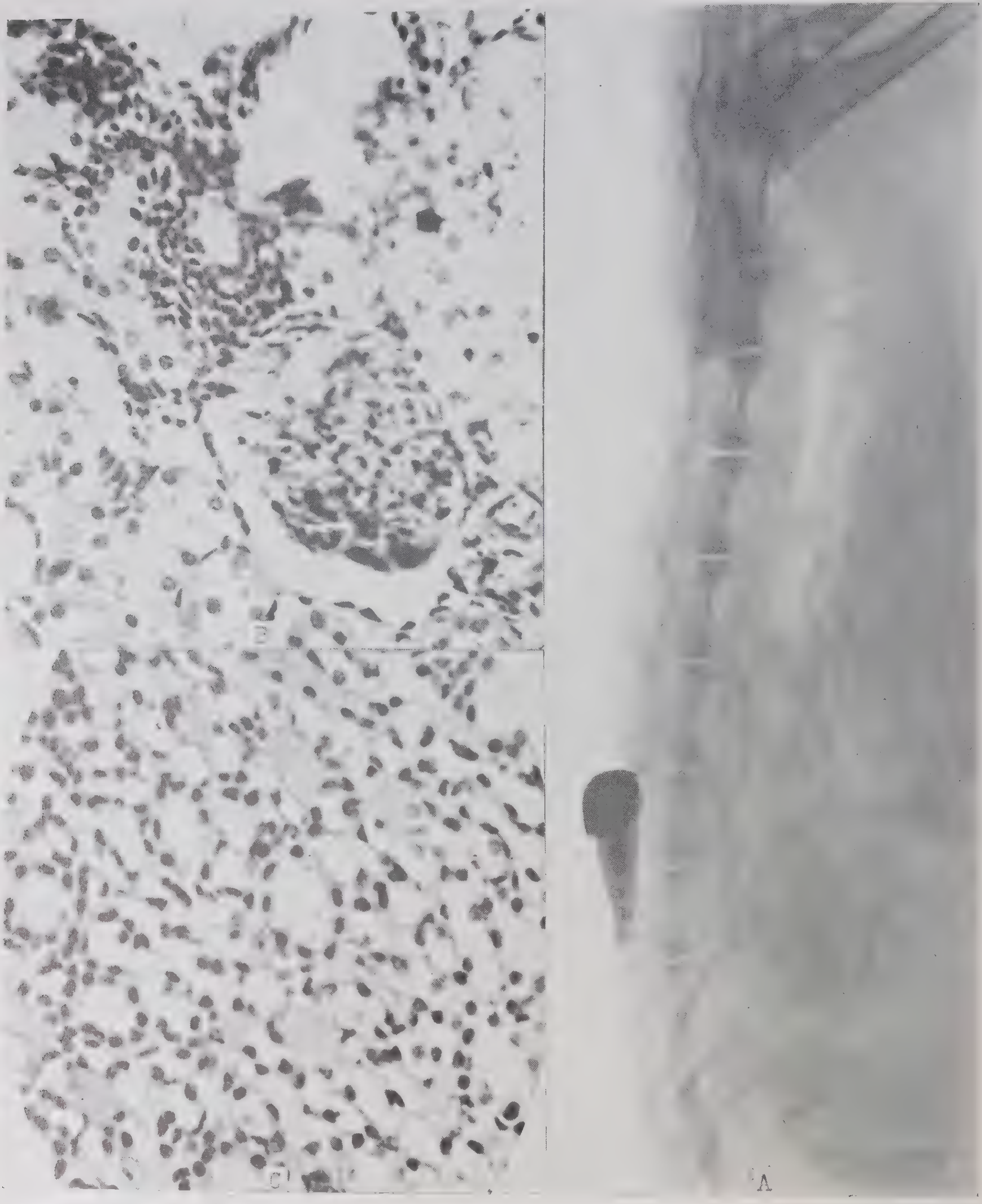


FIGURE 203. A SHOWS, ROENTGENOGRAPHICALLY, A TOOTH IMPLANTED BENEATH THE SKIN OF A RABBIT, WHICH HAD BEEN REMOVED FROM A PATIENT SUFFERING FROM NEPHRITIS. B AND C SHOWS TWO SECTIONS OF THAT RABBIT'S NEPHRITIC KIDNEY WHEN IT WAS CHLOROFORMED SOME WEEKS LATER.

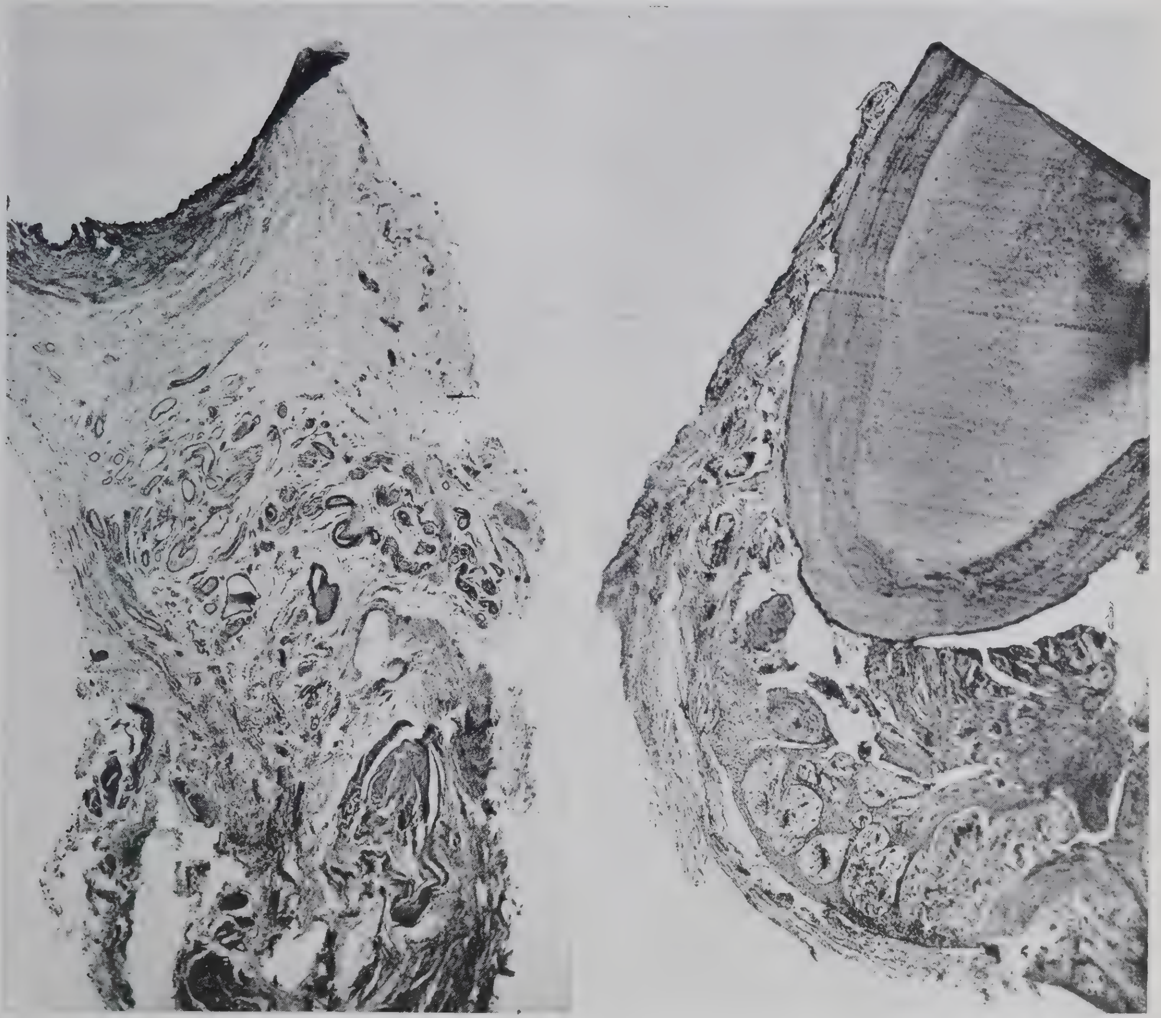


FIGURE 204. TWO GRANULOMATA. THE LEFT WAS DEVELOPED BY THE RABBIT ABOUT THE IMPLANTED TOOTH; THE RIGHT BY THE PATIENT FROM WHOM THE TOOTH WAS EXTRACTED.

not seem justifiable to think of the protective tissue built by the rabbit as a neoplasm; but, if so, why less justifiable so to think of the structure built about the same tooth by the patient from whom it was extracted. With regard to the histological picture presented by a tissue engaged in the process of absorption of the root of a tooth, it will be noted that it is also not possible to distinguish between the structures engaged in this operation, whether taken from the human or the rabbit.

If, then, all rabbits were affected systemically if they did not succeed in building a protective membrane about the tooth, while all survived apparently uninjured if they succeeded in doing so,

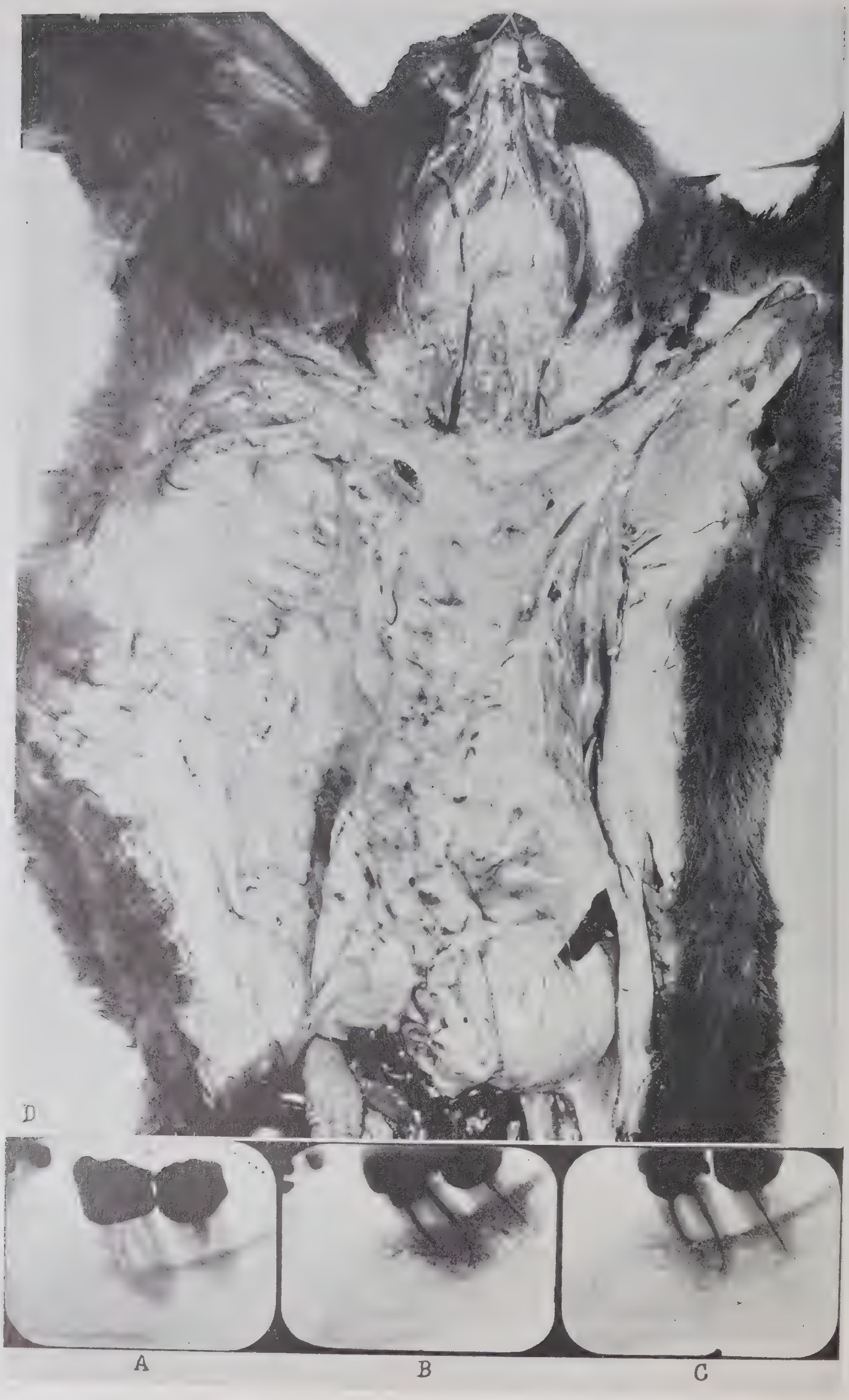


FIGURE 205. SHOWS AN ABSCESS PRODUCED UNDER THE SKIN OF A RABBIT BY THE IMPLANTATION OF A ROOT OF THE MOLAR SHOWN IN C. SEE TEXT.

we find to this extent a co-operation of our interpretations as made in preceding chapters. But this is not all the evidence herewith developed. It may be argued that while a tooth does not furnish either teacupfuls or quarts of organisms, there is still too great a quantity of infection for a rabbit to neutralize. If this be true, one rabbit should neutralize some part of the infection and toxin of a given tooth, and if that tooth should be transferred immediately to another healthy rabbit, we should expect that soon all of the poison in that tooth could be neutralized by the several rabbits. Assuming that an individual is twenty times as large as a rabbit, twenty rabbits might be expected to furnish enough neutralizing power to destroy this activity, whatever it may be in a given tooth. This has been tested incidentally in connection with another problem in which the same tooth was planted beneath the skin of thirty different rabbits, twenty not proving to be sufficient, and the last dying in as short a time as the first, and all but one within six days after the tooth was placed beneath the skin of the rabbit. One lived ten days and it was an exceedingly large and vigorous male who was so ugly a fighter that he tried to kill any other males that were put into the same cage. Within six hours after the tooth was planted beneath the skin, all this pugnacity and viciousness had disappeared, and in a couple of days the typical blood changes with loss of weight appeared.

In the chapter on calcium in relation to dental infections I have referred to the fact, that the ionic calcium of the blood of individuals affected with dental infections, is practically always depressed at the time that they are suffering from rheumatic group lesions; and, further, that if the patient's tooth be placed in the serum of that patient's blood, the ionic calcium is still further and very rapidly lowered, in some instances almost entirely removed from the serum. It can be regained by chemical procedure, as I have shown, for it is apparently in what I have termed a pathologically combined state with the toxin from the tooth. In these rabbits in which teeth have been planted beneath the skin, there has been a marked difference in the change of ionic calcium of the blood whether the animal succeeded in building an encapsulation about the tooth, in which case it generally lived for weeks or months, or whether it was unable to do so. In the former the ionic calcium remained practically constant and normal, while in the latter it was always reduced. With the reduction of the ionic calcium there was always a loss in weight of the animals and the decline was practically in direct proportion to the depression of the ionic calcium, so much so that we could tell almost precisely when a rabbit would die by plotting the curve as the calcium was going down. This is shown in Figure 136 in the chapter on changes in blood calcium. I have stated, as was shown in very many cases in our rabbit posts, that invariably if the rabbit failed to build quickly an encysting membrane about the tooth, death followed promptly and practically always within ten days, in the majority of instances in five days or less, and often within two days. We can scarcely imagine a concentration of poison so profound that the small quantity that would be present in an ordinary root-filled tooth could overwhelm thirty rabbits in succession from a single tooth, and in which all the other teeth from that same patient produced the same effect. We are evidently dealing here with forces that are different from those that enter into our ordinary conception of cause and effect. In preceding chapters I have shown that by washing the crushed tooth and passing the washings through a Berkefeld filter and having a small quantity of apparently clear water left, I would have a substance which, when inoculated into the rabbits, would frequently start them on a decline, even though it was bacteria-free as proven by culture, and which decline would frequently terminate in death in a few weeks, and practically always with a depression of ionic calcium and of body weight.

In the chapter on the efficiency of root fillings (Figure 105) I have shown a case where a tooth, the second molar, was root-filled by us a year previously because we considered it a favorable condition to sterilize and root-fill. The roentgenograms of these teeth and one of the rabbits with the root implanted are shown in Figure 205. A shows the tooth before treatment and root filling, B immediately after root filling, and C seventeen months after root filling. The results of the root filling were quite satisfactory in accordance with the teachings available for the profession at this time. Roentgenographically the very slight zone of rarefaction at the apex of the root had grown less. But the patient was not as well as she should be, with symptoms which I suspected might be related to this tooth; and because of the great improvement she had had from other extractions, she desired to have it removed. This we did. The two roots of this molar were placed beneath the skins of rabbits. One root, the mesial, evidently contained much more toxic substance than the other for, as shown, the first rabbit died in six days. The subdermal abscess is shown in Figure 205-D. The tooth was replanted in another rabbit which died in eleven days. Before it was replanted and after it had killed the first rabbit, I drilled into the apex at the foramen of the tooth after sterilizing the surface (these teeth are always thoroughly cleansed externally before being transferred to another animal) and cultured the borings and found that they contained a pure strain of streptococci, notwithstanding the splendid appearance of the root filling. The rabbit in which the other root, the distal, was implanted was able to encapsulate it. It died in twenty-three days. This root was then transferred to a second rabbit and it in turn encapsulated the root and died in thirty-seven days.

It should be noted that the second rabbit in each of these cases lived much longer than the first, which has a direct bearing on a criticism of this work, which I refer to elsewhere, to the effect that I was overlooking the fact that animal passage makes infections more virulent, which accounted for the more rapid death after the first implantations in the case which was under discussion: namely, where I had drilled several small openings through to the interior of the tooth to permit more free exit of the toxic and bacterial substances. (See Chapter 17, on Quantity, Systemic Effect, and Tooth Capacity.)

The mesial root was again planted beneath the skin of a rabbit and it died, spontaneously, in five days; and still another implantation was made and the rabbit died in four days. Each one of the rabbits developed, besides the large subcutaneous abscess, such lesions as hyperemia of the myocardium, liver, and kidneys, acute myositis and atrophy of the chest and abdominal muscles, all with emaciation. The four rabbits into which the mesial root was planted lived on an average six and one-half days and had an average actual loss in weight of 256 grams, or 20 per cent, and an average loss per rabbit per day of 3.3 per cent. The two rabbits treated by planting the distal root, subdermally, died spontaneously in an average of thirty days, with an average loss of weight of 478 grams, or 31 per cent, or 1 per cent per rabbit per day.

The mesial root was then boiled for ten minutes and placed under the skin of a rabbit, which rabbit is still living at the time of this writing, fifty-one days after implantation. Apparently, the boiling did something to this tooth, for, whereas the other rabbits failed rapidly and died apparently from the effect of having this tooth implanted, this rabbit has gained from 852 grams to 1080 in the fifty-one days, a total gain of over four grams per day. This rabbit, therefore, has had a gain of weight of 21 per cent in fifty-one days, or 0.4 per cent per day. It should also be noted that this rabbit had the same surgical shock that the others did. I desire to warn that it is not fair to conclude, however, that this method of treating suspected teeth—namely, to remove them and boil them and replace them—will always be as adequate as this, since, as I have shown elsewhere, these teeth often contain a toxic substance which is thermostabile and which continues to do some, though less, injury even after the tooth has been boiled.

These facts strongly suggest that the structure that is built about the root of an infected tooth is not a neoplasm, but that it is a protective membrane placed there by Nature to maintain a quarantine and thereby protect the animal or person carrying it. With this in mind, we have made a careful analysis of the condition of this tissue about the root apex in the various types of individuals presenting, and we have found that the type of tissue shown in Figure 198 of this chapter, is practically always present in individuals without rheumatic group lesions or apparent systemic affect from dental infections which they are carrying; and that if this normal high defense which has enabled them to produce this type of quarantine has been broken, there is a definite degeneration of this organ surrounding the apex of a tooth, and it takes on a condition such as that shown in Figure 197, which is the typical clinical state of the granuloma as found in individuals with a broken defense; and, further, that in those individuals, who have a chronically low defense, there is never an ample effort made to build such a quarantine station about the tooth. It is not well organized nor extensive in quantity, and we frequently, if not generally, find free organisms between this tissue and the root end. This type is illustrated in Figure 199. From a bacteriological standpoint in the individuals with either a chronically low defense or a recently acquired loss of defense (those with acquired susceptibility), we not only have the lack of well vascularized defensive tissue, but we have the definite evidence of infection in the form of organisms and very few phagocyted leucocytes; whereas in the periapical tissues of the individuals who have at that time an ample and high defense, we not only find a complete absence of organisms, but we do find both a highly vascularized tissue and the tissue elements necessary for an active defense: namely, many leucocytes, some of them phagocyted.

An illustration of one of Nature's mechanisms is shown in Figure 198-A and B. This shows in A the relation of the periapical defensive tissue to the root apex. It will be noted that there is little depression in the granuloma just over the exit of the apical foramen. This is shown highly magnified in B; and it will be noted that it is lined with a vigorous membrane of columnar epithelial cells, each with a well defined nucleus, and all of which have taken the stain vigorously, showing evidence of splendid vitality; and this seems to be the first line defensive tissue, for it is the type of tissue that Nature has built throughout the alimentary tract to defend us against the absorption of bacterial toxins. It is not strange that Nature should use the same effective mechanism here which she does in that extensive portal for bacterial and toxic entrance into the system.

If, then, as these data suggest, the dental granuloma so-called is not a neoplasm—in other words, is not a pathological tissue but a physiological tissue, whose function is to defend the individual against bacterial and toxin invasion,—we should have evidence of this quality by other means of observation. To test this I have placed various types of granulomata in both suspensions of organisms and freshly infected culture media with the remarkable result that whereas in the tube with the degenerating granuloma there is very little power to destroy bacteria in its vicinity, the vigorously functioning, freshly removed granuloma destroys the organisms in its vicinity in its tube, or at least there is developed a clear space in infected culture media for some distance surrounding the granuloma tissue. A bacterial count of the total fluid in the tube with the well organized granuloma shows a reduction from one-half to one-third that of the control tube.

A vigorously functioning granuloma should develop about the root of a tooth, carrying either a considerable quantity or a very toxic infection, such quantity as develops in practically any tooth providing the capacity of the dentin for bacterial growth and in addition the pulp chamber; and any patient who has this quantity of infection and does not produce such a defensive mechanism is not only in danger of being early affected, but in most instances is already being affected by the contents of that tooth. Such a condition is shown in Figure 206. This patient has carried this tooth for years. It has a fistula and he is in splendid health.

It is a most remarkable fact that when we study our old people who have lived through all the overloads incident to life and ex-

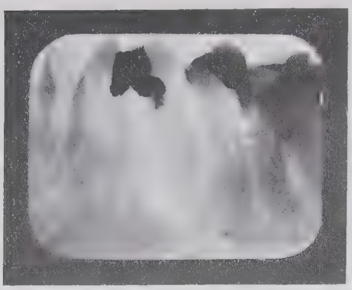


FIGURE 206. A VIGOROUSLY FUNCTIONING GRANULOMA IN A PATIENT OF A HIGH DEFENSE.

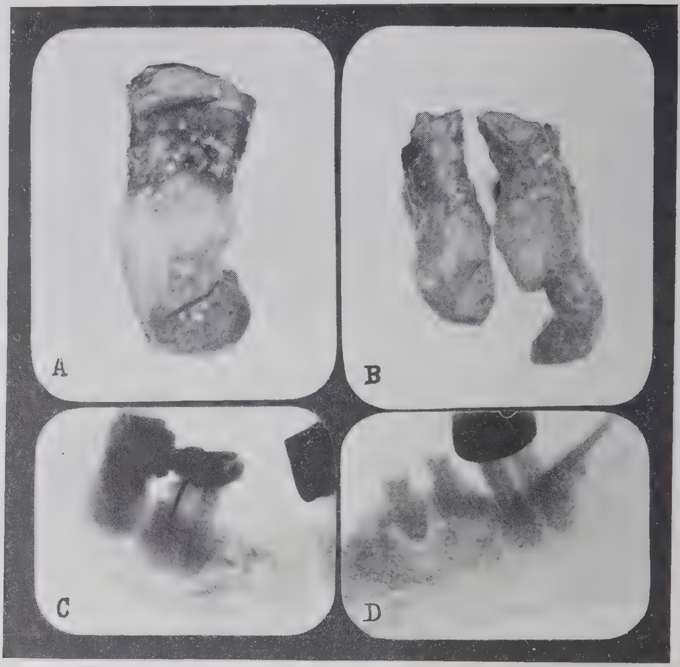


FIGURE 207. THE ROENTGENOGRAPHIC AND PHOTOGRAPHIC VIEWS OF GRANULOMATA WHICH PROTECTED THE PATIENT UNTIL ABOUT EIGHTY YEARS OF AGE.

tensive dental infections, and who in spite of them all and, particularly, in spite of what seemed to be extensive dental infections, are still well or relatively so for their age, we find this type of reaction about the roots of teeth. Such a case is shown in Figure 207. This patient, about eighty years of age, has several such teeth as this. C and D show the roentgenographic appearance of these two teeth, the lower right second molar and lower left second molar. Throughout her lifetime she has never suffered from neuritis, rheumatism, or nervous breakdown; and, incidentally, those disturbances are practically unknown in her family. A full set of roentgenograms of her case and also her brother's is shown in Figure 34 Chapter 3. When we study these teeth in connection with Nature's quarantine—namely, this vigorous, well vascularized, periapical encapsulation,—we see why she has had her protection. Incidentally, however, she has developed recently a kidney irritation which has entirely disappeared with the removal of these dental infections. Even her splendid defense has lately been breaking.

We do not yet know the full meaning and function of the epithelial structures which Nature builds into these highly efficient quarantine stations, but it seems very evident that it is not acci-

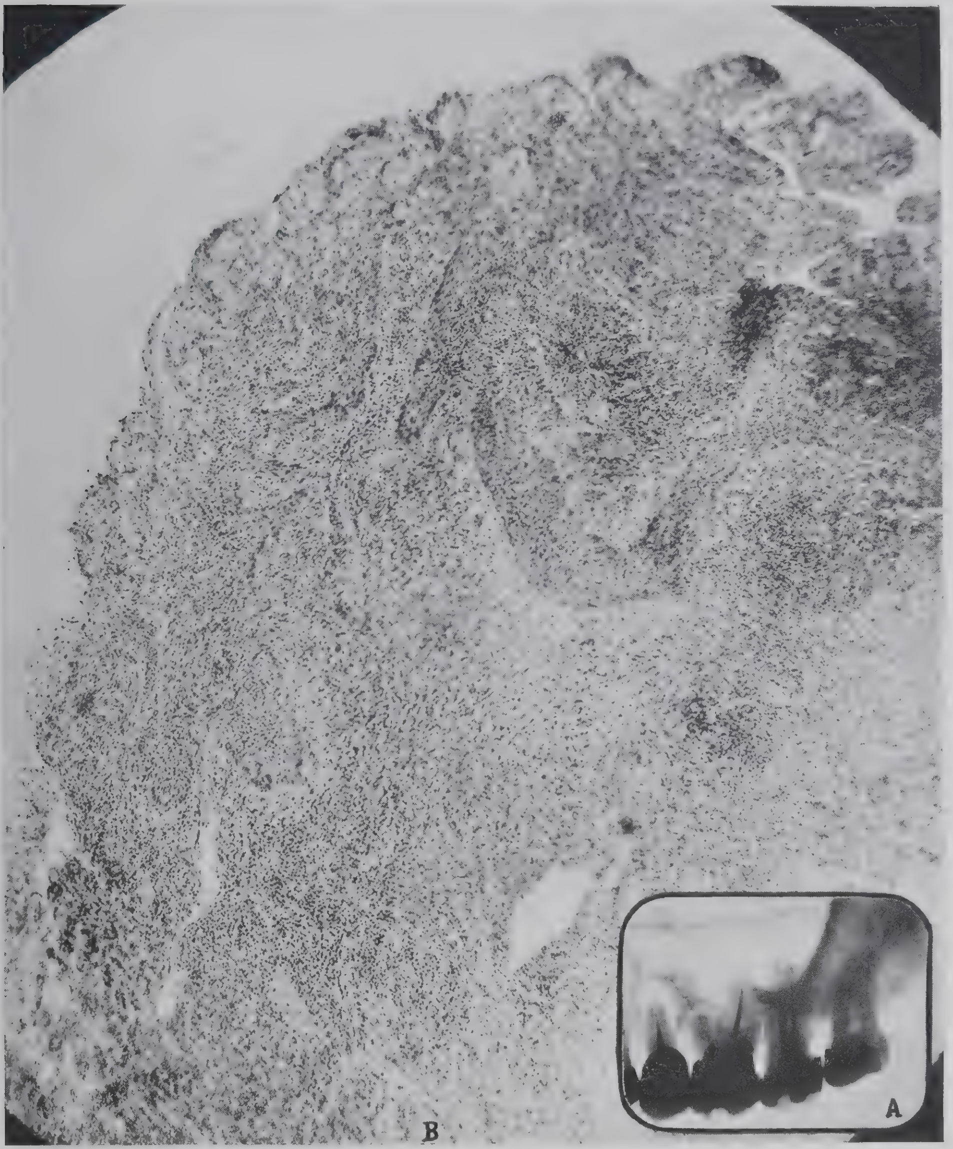


FIGURE 208. A HIGHLY FUNCTIONING GRANULOMA. NOTE THE LARGE AMOUNT OF EPITHELIAL TISSUE.

dental that this structure, when most efficient, carries a very large amount of epithelial tissue. This is illustrated in Figure 208, which is from the tooth of a patient with exceedingly high defense, the roentgenographic view of which is shown in A. It should not be presumed, therefore, that those individuals, having a high defense, as expressed by their capacity to build an efficient quarantine station about an infected root, are safe both for the present and future. To test this I have planted teeth in rabbits,

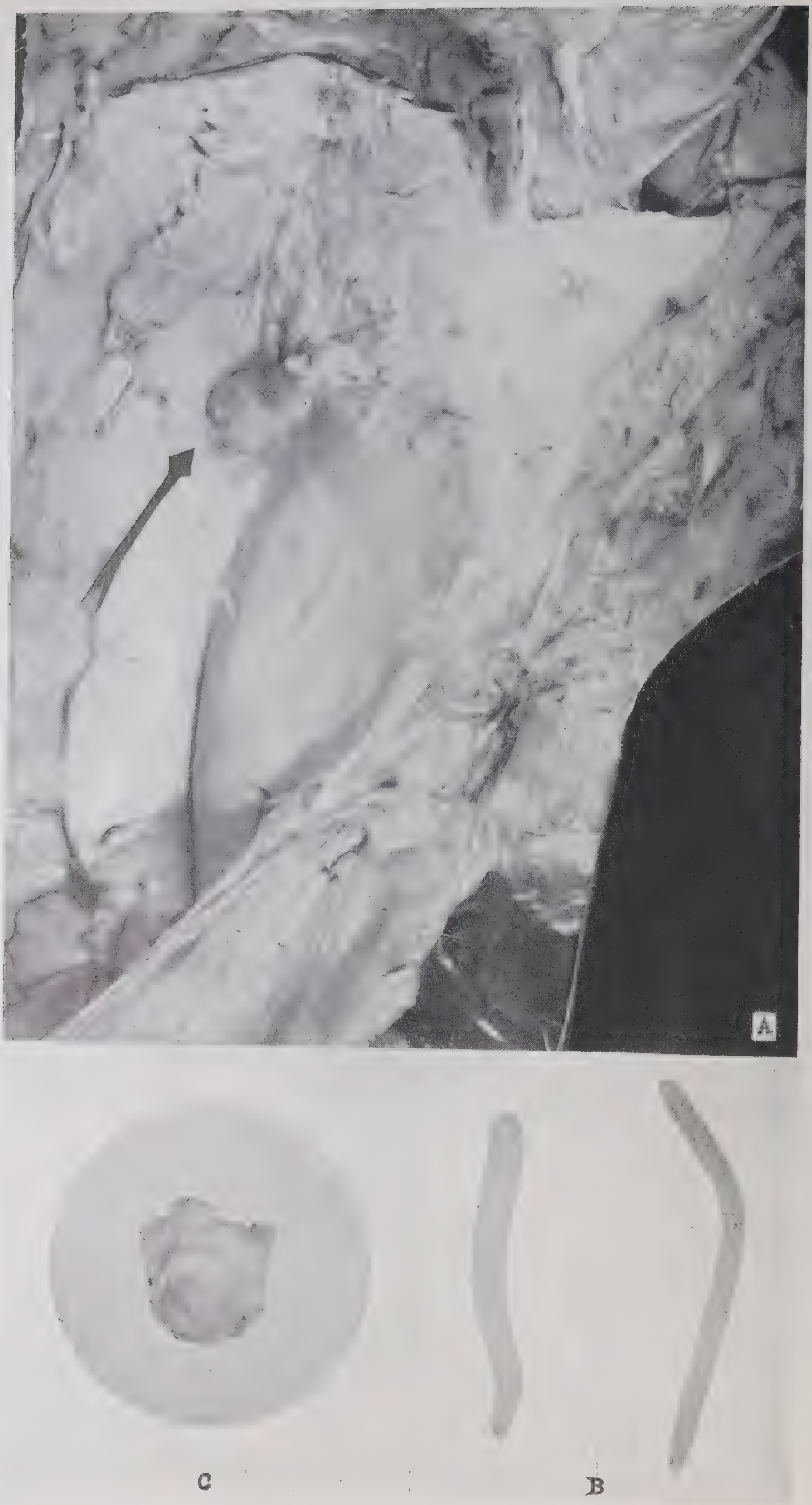


FIGURE 209. AN IMPLANTED TOOTH WHICH THE RABBIT CARRIED THIRTEEN MONTHS. IT DIED OF NEPHRITIS, FROM WHICH THE PATIENT WAS SUFFERING. C, THE ENCAPSULATED TOOTH; B, CASTS FROM THE RABBIT'S URINE.

and where they had built a high defense I have kept them under favorable conditions for long periods to see what the effects would be. Recently two of such test rabbits have died with nephritis, where the teeth had been implanted over a year previously and about which the rabbits apparently built adequate defense but in which contest the rabbit finally lost the fight. Figure 209 shows in A a dissection of a posted rabbit where a large broken down cyst is shown. It is remarkable that the animal gained from 975 grams

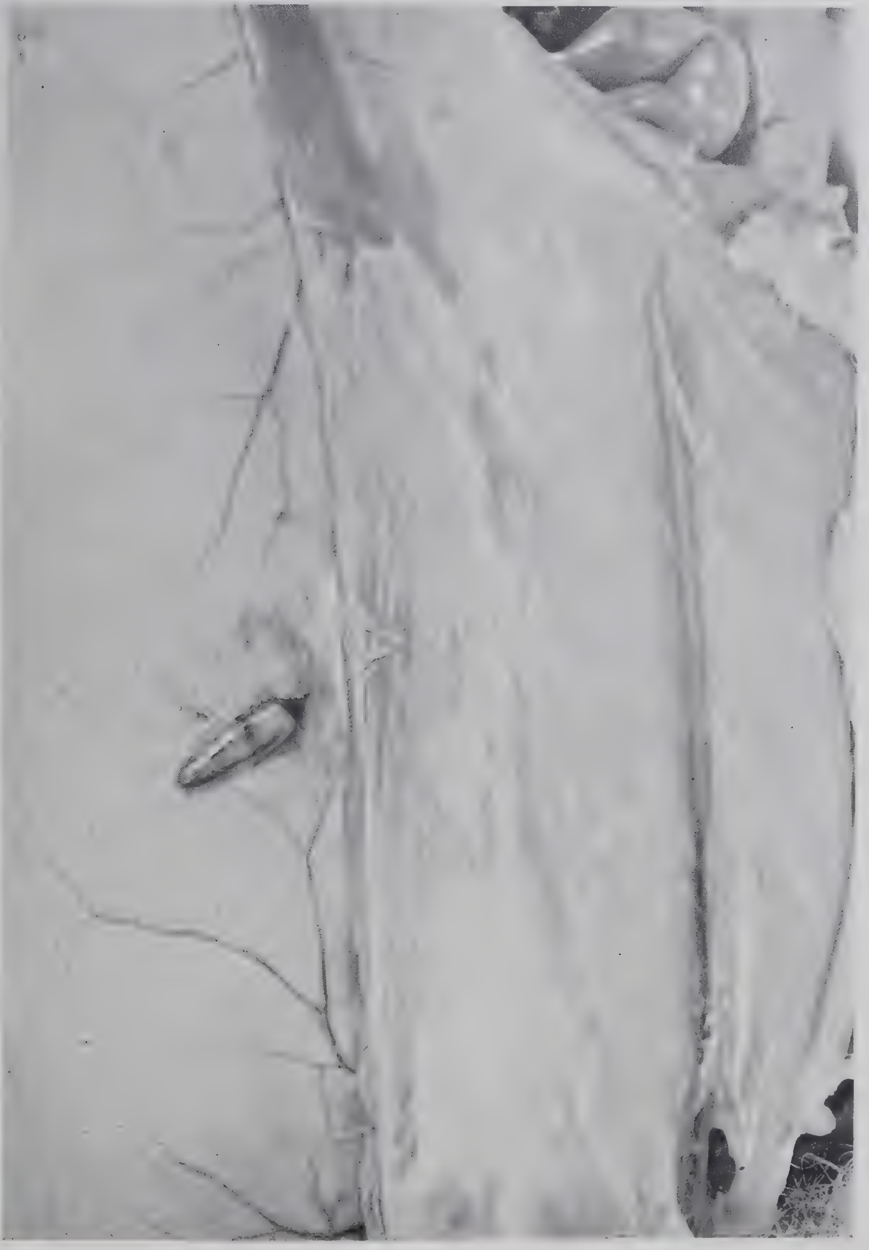


FIGURE 210. A STERILE IMPLANTED TOOTH WHICH PRODUCED PRACTICALLY NO ENCAPSULATION.

to 2885, nearly three times its original weight, in eight months, when it started to decline, and died thirteen months after the implanting of the tooth, with a weight of 2010 grams, having lost from its maximum weight 875 grams, or 30 per cent. Figure 209-B shows casts from this rabbit's urine, and C shows the encapsulated tooth. It is important to note that this patient was suffering from acute Bright's disease at the time of the removal of her tooth.

It is very important to note the very great difference in the local structural changes about a tooth which may stay for a long period of time under the skin of a rabbit and produce no evidence of injury to the rabbit. Whereas in the last case the tooth, which was potentially able, we believe, to do injury to both the patient from whom it was taken and the rabbit, was tolerated for a long time by the rabbit, it had built about it a very vigorous and well vascularized defensive tissue. When sterile, non-irritating, foreign substances, as illustrated in the coin in Figure 201, are planted beneath the skins of rabbits, there is not only no systemic disturbance, but there is practically no local reaction. This is what happens also when teeth that are implanted are free from irritating substances. In other words, they lie in the tissue without encapsulation, covered only with a membrane so thin and transparent that the tooth can be seen almost as perfectly as if it were not encapsulated. Such a tooth is shown in Figure 210, which remained in a rabbit for sixteen months, when the rabbit was chloroformed to study its structure. During this time it had gained progressively from 1603 grams to 3034. This tooth was removed from the patient not because of roentgenographic evidence that it was in error but as a matter of precaution, the patient having had a serious injury from a previous dental infection. It is my belief that this tooth was not injuring this patient.

In a previous paragraph of this chapter I discussed the fact, that even boiled teeth seemed to contain toxic substance. It is quite important that, whereas implanted teeth that are apparently entirely free from infection, such as some of our surgically removed impacted third molars, produce practically no encapsulation such as the last tooth showed. The boiling, or even autoclaving, of teeth does not always destroy all the toxic substance. We do not yet know the full significance of this except that the toxin seems to be thermostabile and we have found evidence of this, (as shown in Chapter 30 on Sensitizations, where the extract taken from teeth was found to produce the typical intradermal skin reaction) in many instances, each when passed through a Berkefeld filter, when sterilized chemically, when boiled for an hour, when autoclaved at thirty pounds, and also when autoclaved at three hundred twenty pounds for two hours. I was, therefore, not surprised to find that there was a distinct difference in the reaction locally and on animals when boiled teeth had been infected. Boiled and autoclaved infected teeth have encapsulations developed about them almost invariably. But this is not the most important part of it. Very often the rabbits carrying these teeth show blood changes within a couple of weeks and begin losing in weight. Figure 211 shows the typical appearances of the encapsulations about three such boiled teeth. A was boiled for one hour. The rabbit (No. 1165) died in twenty days, with a loss of 160 grams, or 9 per cent. It is impossible to state definitely to what extent the tooth contributed to the rabbit's death. B (Rabbit 1189) died spontaneously in twenty-two days, with a loss of 149 grams, or 15 per cent. The tooth was boiled for two hours. C was autoclaved at thirty pounds pressure for one hour. This rabbit (No. 1171) was chloroformed in six days, as it was nearing death, with a loss of 332 grams, or 31 per cent. It is therefore apparent that these infected teeth contain a substance which has a direct action on metabolism. This rabbit, having

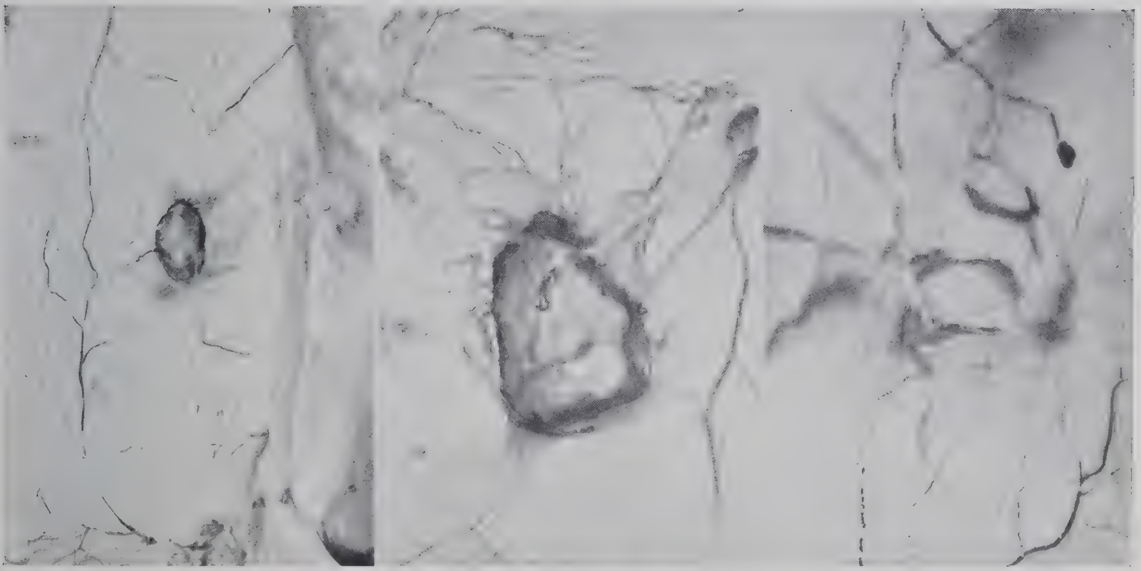


FIGURE 211. ENCAPSULATIONS ABOUT BOILED INFECTED TEETH. HEATING DID NOT DESTROY THE TOXIN.

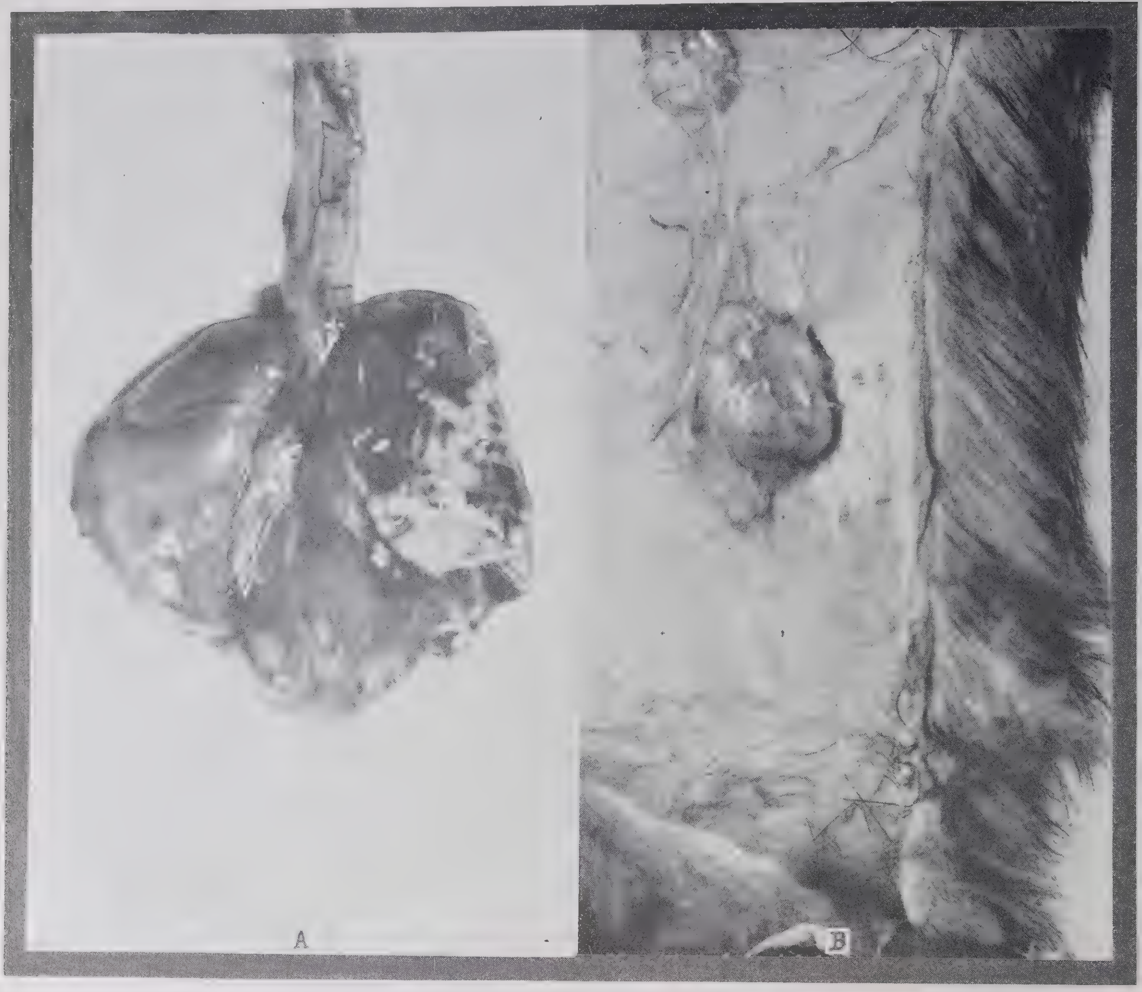


Figure 212. One of several rabbits which developed pneumonia following the implanting of an infected tooth. A, pneumonic lung; B, the encysted tooth.

lost this large amount, was rapidly approaching death; and, in order to secure the blood before any postmortem changes could take place, it was chloroformed; and while under chloroform before death, sufficient blood was aspirated from the heart to make our blood calcium determinations. In this rabbit the ionic calcium was approximately normal, 10.7, and it, apparently, had not undergone the same structural changes of the blood that those rabbits did which had this same tooth planted beneath their skins before it was boiled but with its normal infection as taken from the patient.

A further and striking evidence of the toxicity of these infected teeth and of the nature and stability of this toxin, is shown in the fact that frequently the rabbits carrying these implanted teeth die of pneumonia. Such a case is shown in Figure 212. This rabbit had a tooth planted which had previously killed several rabbits by subcutaneous subdermal implantations, but before this implantation it was autoclaved for one hour at thirty pounds. The rabbit died in thirty-five days and lost in weight 617 grams, or 36 per cent.

It may be argued that in these cases the heating to high temperatures has produced a protein compound that is irritating or poisonous. To test this further we have heated a tooth to 56° for one hour. This should not produce structural change in the protein molecules sufficient to be toxic, and should destroy non-spore forming organisms, which would include the streptococcus. This rabbit died in eight days, with fibrous encapsulation, as shown in Figure 213. It lost 145 grams, or 16 per cent.

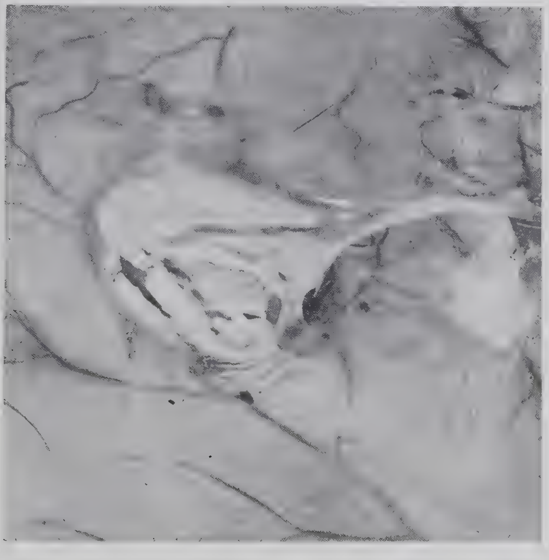


FIGURE 213. TOOTH WAS HEATED TO 56° FOR ONE HOUR BEFORE IMPLANTATION.

The so-called granuloma, for this seems clearly a misnomer, has apparently in these cases destroyed a large number, and in some instances a large proportion, of the bacteria present. To test this further we have placed pieces of such granuloma taken from healthy individuals on agar plates, which had first been inoculated by flowing over their surfaces a suspension of bacteria and pouring off all excess. As shown in Figure 214, while the organisms grew in massive colonies all over the plate, practically no organisms grew for several millimeters surrounding the granuloma, notwithstanding the fact that we might readily expect that its bacteriolytic action should only be available during the time of its vitality.

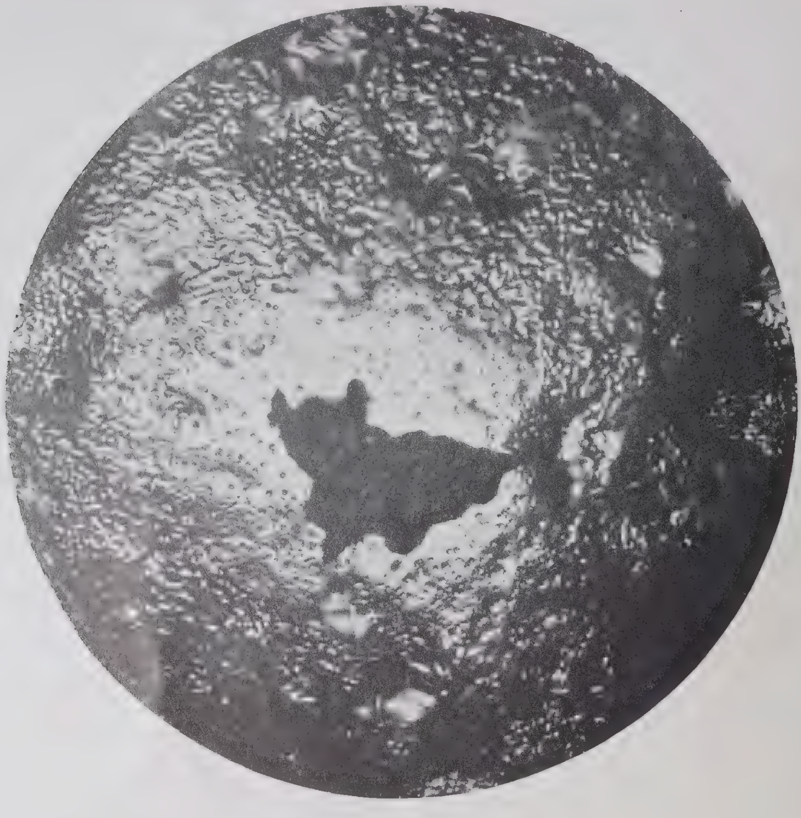


FIGURE 214. SHOWS THE REDUCED BACTERIAL GROWTH IN THE VICINITY OF A WELL ORGANIZED GRANULOMA WHEN PLACED ON AN INFECTED PETRI DISH.

SUMMARY AND CONCLUSIONS.

We would, accordingly, change our interpretation and evaluation of that structure which Nature builds about a root apex. With these data in mind, let us review the findings of Chapter 3 in which, in many instances, the same infection produces an entirely different structural change about a root apex, to what it does in others; and in Chapter 4 that there is a great difference in the susceptibility of individuals to injury from dental infections; and particularly in Chapter 5 that it is those individuals with the large area of rarefaction about the tooth, and hence a large so-called granuloma, who prove to be the persons who, as shown in Figure 200, have a high defense or are free from danger from injury from their dental infections. Since, then, (1) these large areas, as is continually shown in surgical procedure in removal of teeth, contain a more abundant defensive membrane, which type of membrane Nature reproduces in the rabbit, if that same tooth be placed beneath the skin, and thereby protects the rabbit from the toxic substance within the tooth; and (2) since the blood changes as expressed in ionic calcium vary in direct proportion to the ability to build such a membrane, we find no alternative from the following conclusions:

(1) **The so-called granuloma is a misnomer, for it is a defensive membrane and not a neoplasm.**

(2) **A normally functioning periapical quarantine tissue is Nature's effective mechanism for protecting that individual by destroying the organisms and toxins immediately at their source, and thereby completely preventing the tissues of that individual's body from exposure to either of these agencies.**

CHAPTER XXXIX.

CHANGES IN THE SUPPORTING STRUCTURES OF THE TEETH, DUE TO INFECTION AND IRRITATION PROCESSES.

EXPERIMENTAL AND DISCUSSION.

In the preceding chapter, the data have disclosed a wide variation in the structural changes which occur in the supporting structures of the teeth, depending upon the nature and quantity of the irritant or infection, and the capacity for defensive reaction on the part of the individual. In Chapter 3, we saw that either, or both, a rarefying osteitis or a condensing osteitis may be produced about the apex of a root of a tooth; and in Chapter 5, we found that the condition expressing itself in very extensive destruction of bone about the apex of a root, occurs in individuals with a high defensive reaction against the dental infection; that in these individuals, during the time of their high defense, the zone of rarefaction blends into the medullary spaces in a diffuse manner; that when these individuals lose this high defense, the zone not only ceases to become larger, but a fistula, if present, tends to become closed, and a zone of condensing osteitis tends to develop around the zone of rarefaction; and that in those individuals with a low defense for the type of infection always found in dental lesions, streptococcal diplococcal types, not only low at present but for a long period previously, the condition resembles that of the last type except on a much smaller scale in that the zone of rarefaction is usually very much smaller, for a given infection, while the zone of condensation may be very much greater.

I have undertaken to discover somewhat more in detail the nature of these processes, and in order to do so have made extensive dissections of a large number of maxillae and mandibles. A typical illustration of what we have just reviewed in the preceding is shown in Figures 215 and 216, which show in 215 a mandible with two bicuspids and three molars in place, with the buccal plate removed. A couple of metallic wires have been placed through the inferior dental canal, passing out through the mental foramen.

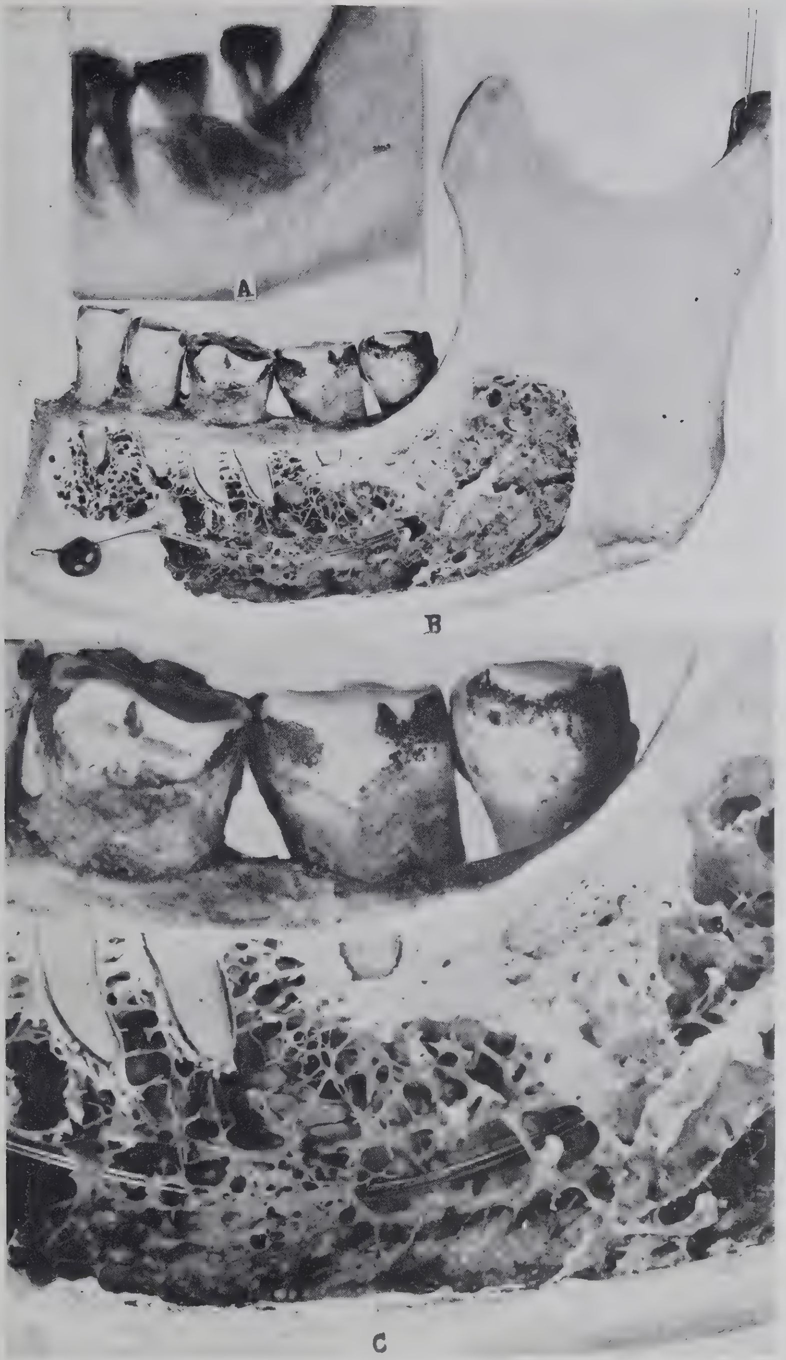


Figure 215. A, the roentgenographic appearance of the dissections in B and C. Note pocket between second and third molars and adjoining radiopacity. B and C show the arrangement of the calcified structures.

Figure 216 shows progressive enlargements of the normal and pathological bone about the molar teeth. (Note: In the various views of this specimen an artefact presents, seen in Figures 215-B and

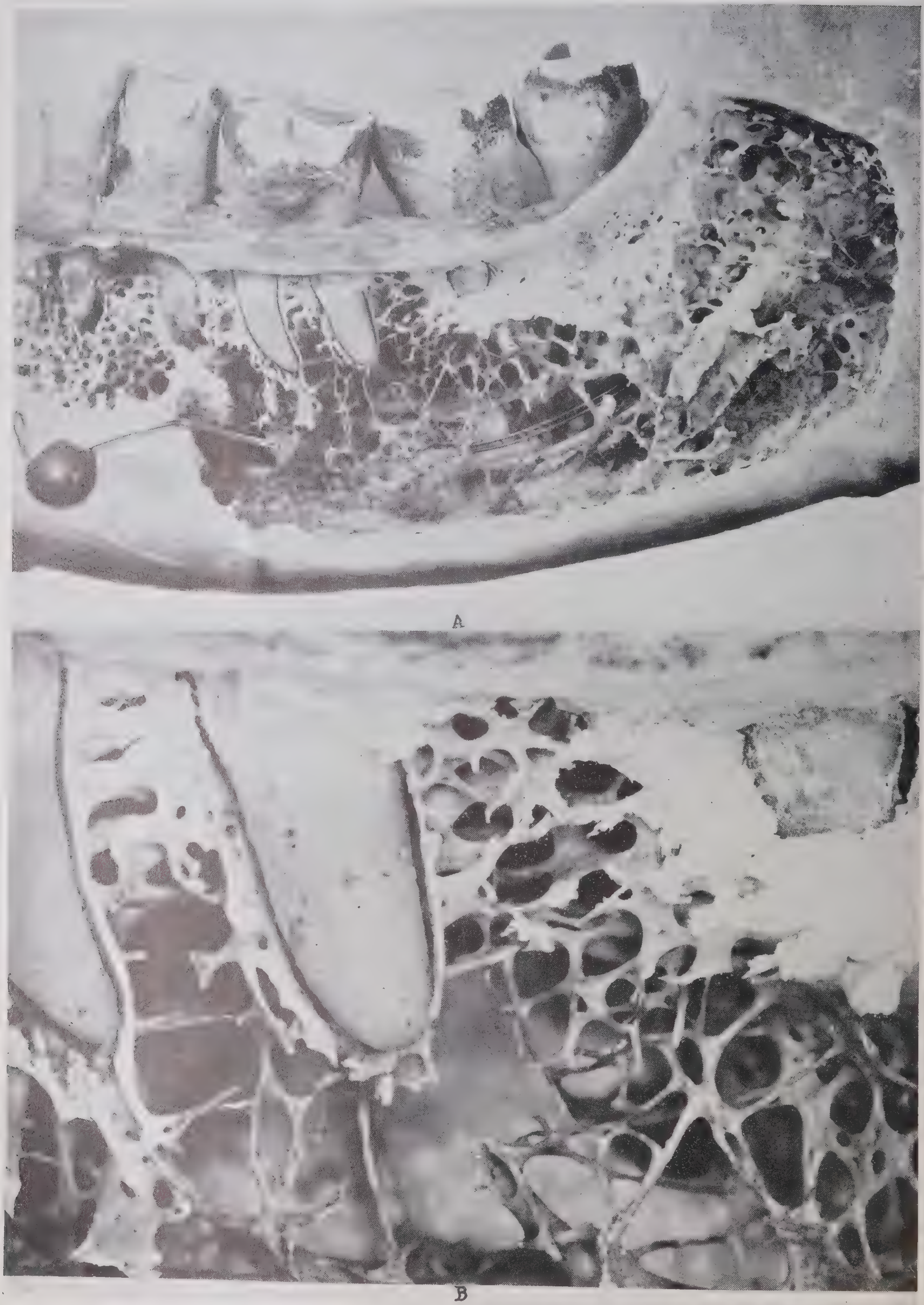


Figure 216. Enlargements of preceding to show trabecular arrangement and condensing osteitis surrounding a periodontoclasia pocket. A late stage.

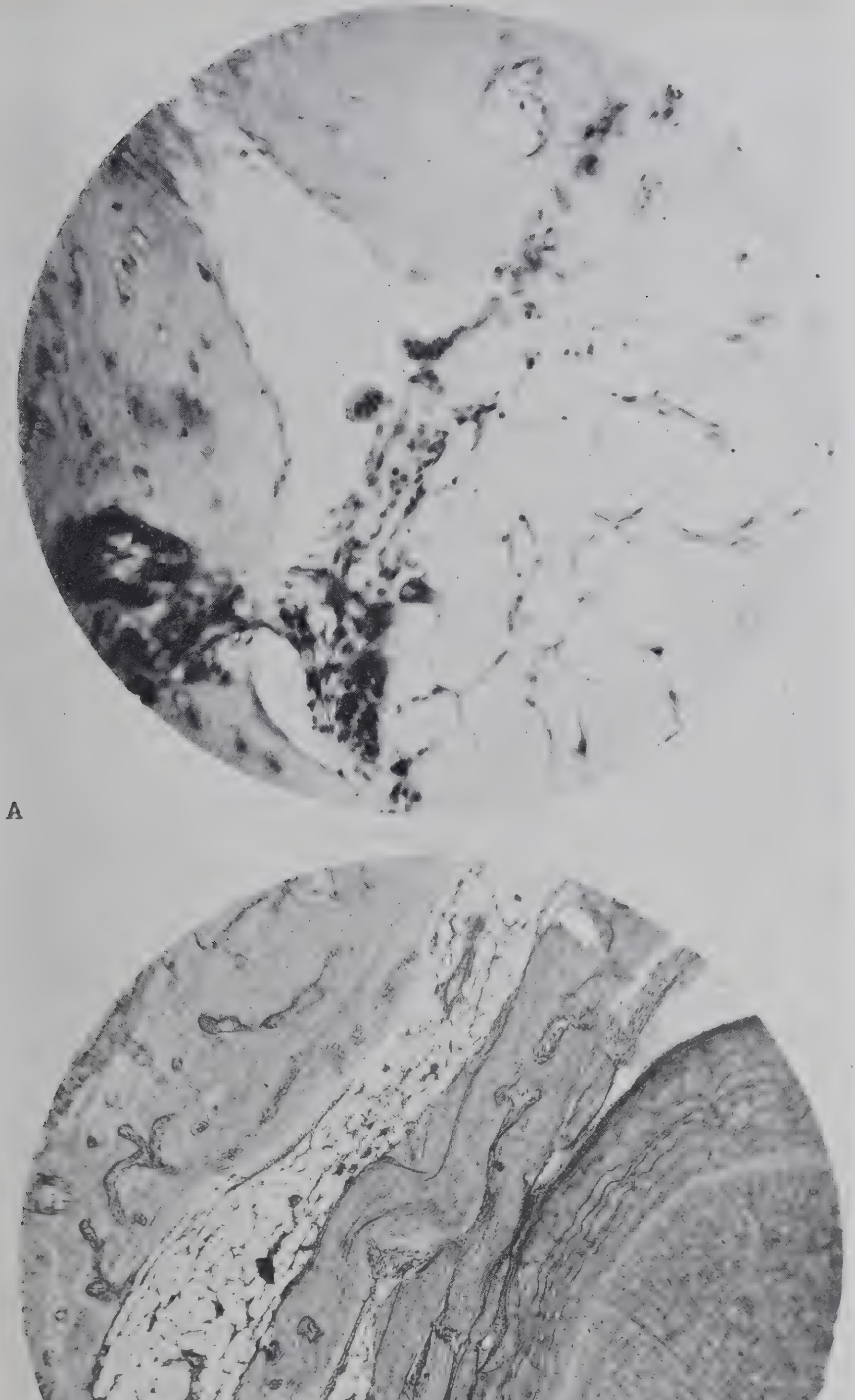


FIGURE 217. A, OSTEOCLASTS IN THE PROCESS OF REMOVING ALVEOLAR BONE IN PERIODONTOCLASIA. B, A CROSS SECTION OF THE TOOTH AND SUPPORTING ALVEOLAR BONE.

216-A. When the tissue was being cleaned the bicuspids were dislodged and were cemented back without care being taken to have them properly seated. What appears to be areas of absorption about the apices of the two bicuspids are open spaces due to the fact, that the teeth are not receded properly in their sockets. There is no pathological absorption; the original lamina dura is present.) Several things will be noted: First, the very porous condition of the normal bone below the bicuspids and first and second molars, and the very dense bone, amounting almost to a homogeneous mass, below the second and third molars. A more careful examination of this case reveals, as shown in the roentgenogram in 215-A, that there is an old periodontoclasia pocket mesial to the third molar, where food was packing; and my interpretation of the condition would be, that this individual's defense had reduced a considerable time before his death; and that with this lowered defense, the active spirochete infection in the periodontoclasia pockets, which had been a participant in the original destruction of the gingival crest and alveolar bone, had largely given way to coccal infections, particularly streptococcal, in the deep tissues, and bacillary forms in the periodontoclasia pockets. The effect of the irritation in the vicinity of this bacterial invasion was entirely different from the process that had occurred earlier in the history of this lesion. At that time, when the patient's defense was high, the cellular activity was so acute that with the stimulation of the irritation, all cell function was high. With the toxic irritation came a very marked dilatation of the capillaries. These poured out their defensive factors, which were markedly alkaline and contained large numbers of leucocytes. These defensive factors were quite ample to establish a quarantine about that local infection, thereby inhibiting the passage of either the bacteria or their products from entering the system. A part of this process involved the destruction of alveolar bone, for the fluids and cells poured into this part were those adapted for the tearing down of alveolar bone as fast as it became involved.

This process of decalcification is so often a physiologic one that it is difficult to distinguish between a physiologic and pathologic absorption of bone. An illustration of this process is shown in Figure 217, which shows in B a cross section of a tooth and the supporting alveolar bone, and in A the giant cells in the deepest part of the periodontoclasia pocket engaged in the process of taking down the hard structures and transporting them in an absorption process. With the development of overloads, whether age, exposure, or disease, the defense of all individuals goes down; and in Figure 215, we see a zone of very dense bone where the trabecular structure is almost completely obliterated. If we would compare the bone formation about the roots of the first molar with that of the second and third molars, we would find a very striking difference. This is shown in higher magnification in Figure 216. Note that the lamina dura about the roots of the first molar is the thin shell supported lightly by trabeculæ of small size, which form almost a lace-like network in the body of the mandible. Note where a section of the cancellous osseous structure is broken out below the apex of the distal root of the first molar, that there is an open osseous channel exposed, through which the blood vessels and nerves entering the distal root of the first molar pass protectedly in a tube through the medullary matter up to the root apex. This condition is also shown in the osseous structures leading to the mesial root of the first molar.

The roentgenographic study of this condition is shown in A of Figure 215, and reveals the following: a zone of condensation or radiopacity about the second and third molars and a normal cancellous bone about the first.

Before proceeding with the discussion of these structural changes, I wish to call attention to the fact that, in preceding chapters, I have frequently spoken of the fact that teeth and their sockets of individuals with normally high defense, and particularly those with abnormally high defense, respond very differently in the various surgical procedures, operative and postoperative. For example, it will readily be seen why it would be very easy to infiltrate an anesthetic into the supporting structures of the bicuspids, while it would be relatively difficult in these molars; and also with a highly vascularized medullary fat filling the interspaces between the trabeculæ about the bicuspid roots, it would be exceedingly easy for Nature both to combat infection and repair tissue, as compared with her facilities and ease for carrying on that function in the case of the molar roots. The vascularization is gone, largely, in the latter case. It would be much more difficult to extract a root in this latter condition and it would readily be understood why the old process would be very much more delayed and interrupted in this latter condition; and, indeed it could easily be understood why Nature might desire to throw

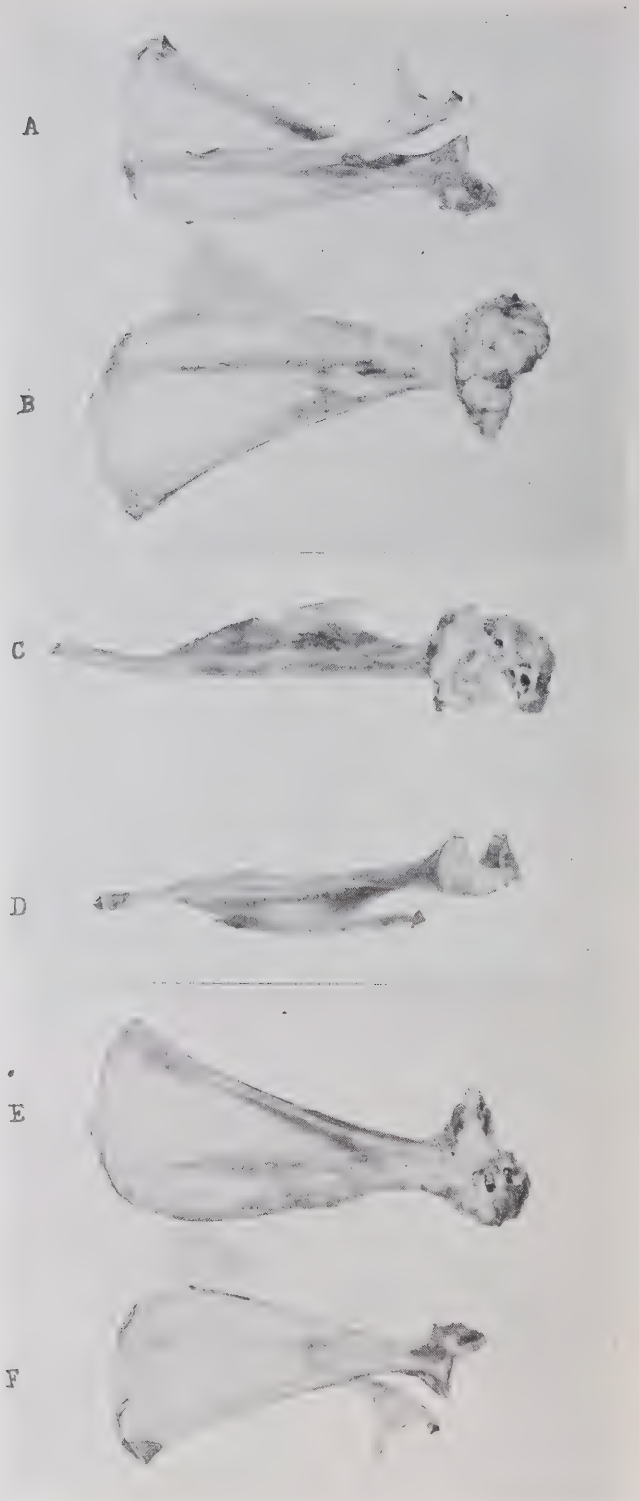


Figure 218. A proliferative arthritis in a rabbit's shoulder. A, D, and F show normal scapulae; B, C, and E grossly deformed.

off as a sequestrum a large or small part of this condensing bone.

But our process is not limited in this instance to the irritation of infection entering the original exposed and necrotic bone, for the presence of that infection has, as we have shown in Chapter 8 on Periodontoclasia and Pulp Involvement, in all probability, injured the pulps of these teeth.

There is another and very important phase of this problem which has not received proper consideration, which is the reaction of the infection from near or distant parts of the body on the supporting structures of the teeth. In the preceding discussion, we have almost entirely limited our considerations to the effect of dental infections on the immediate adjoining dental and supporting structures, and upon other tissues and organs of the body. Since a tooth is suspended in a socket in such a manner as to make a movable joint, it and its supporting structures are subject to many of the structural changes to which any or all joints may be susceptible. In order that we may understand, somewhat, the nature of this process, we will approach it by a consideration of the changes which take place in the joints. These may be, in general, divided into two main groups which we will refer to as degenerative and proliferative processes. Each of these will produce deforming arthritis. In the first there is marked ankylosis, lack of mobility, and with removal of the dental infection or other source of irritation which has been largely instrumental in furnishing the toxic and infective processes for its development, there may be a cessation of inflammatory process with fixation, a more or less permanent ankylosis, but often with quite complete freedom from pain. These individuals may live for years, not infrequently twenty or thirty, with many or nearly all joints of the body immobile. In other instances there is a slow reparative process. In the second group, with the degenerative arthritis, there tends to be a destruction of synovial membrane, with destruction of the cartilages and often with marked absorption of the bone. These two types are shown reproduced in rabbits in Figures 218 and 219. It is important to note that in our animal studies we have found that strains taken from some teeth tend quite regularly to produce in rabbits the former type, while strains taken from teeth of other patients inoculated into rabbits produce changes of the latter type. We will discuss this in further detail in a later communication.

A minute study of the pathological changes will be seen in the

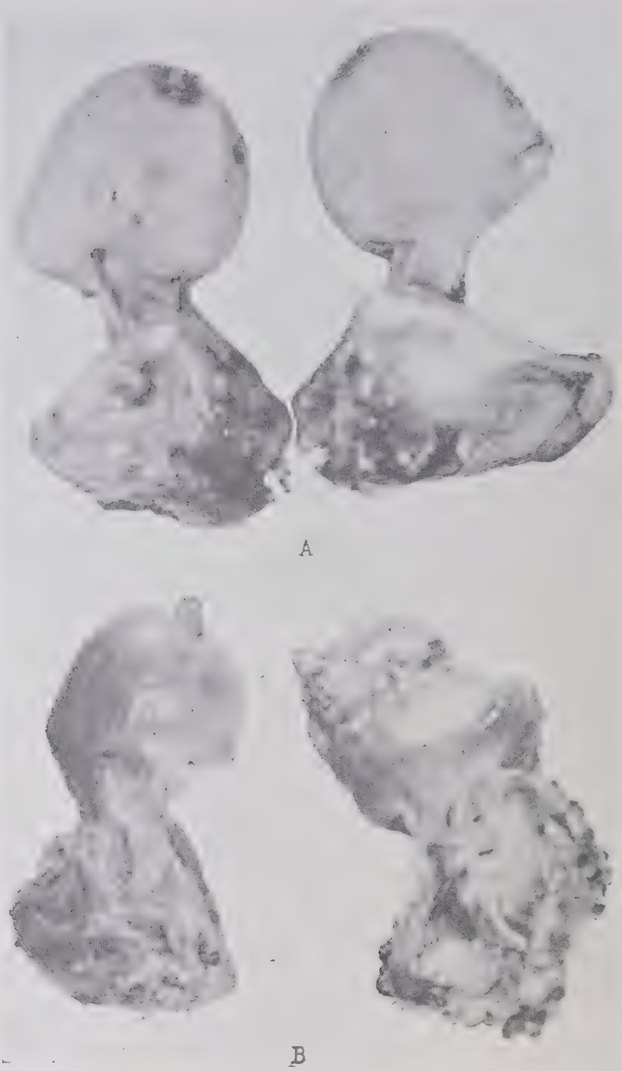


FIGURE 219. A DEGENERATIVE ARTHRITIS IN A RABBIT'S HIP JOINT. A, NORMAL HEADS OF FEMORAE; B, DESTRUCTION OF ENTIRE ARTICULATING SURFACE.

following figures. Figure 220 shows a section through the knee joint of a rabbit suffering from acute rheumatic infection resulting from a minute inoculation in the ear vein. It will be noted that the inflammatory process has attacked the trabecular structure and also the cortical layer beneath the synovial membrane. The synovial membrane is itself seriously attacked in some places, as shown in Figure 221. It will be observed that the degeneration is extending through this membrane into the cortical layer. The tissues of the knee shown in Figures 220 and 221, were cultured and a diplococcus was isolated which was also shown in direct

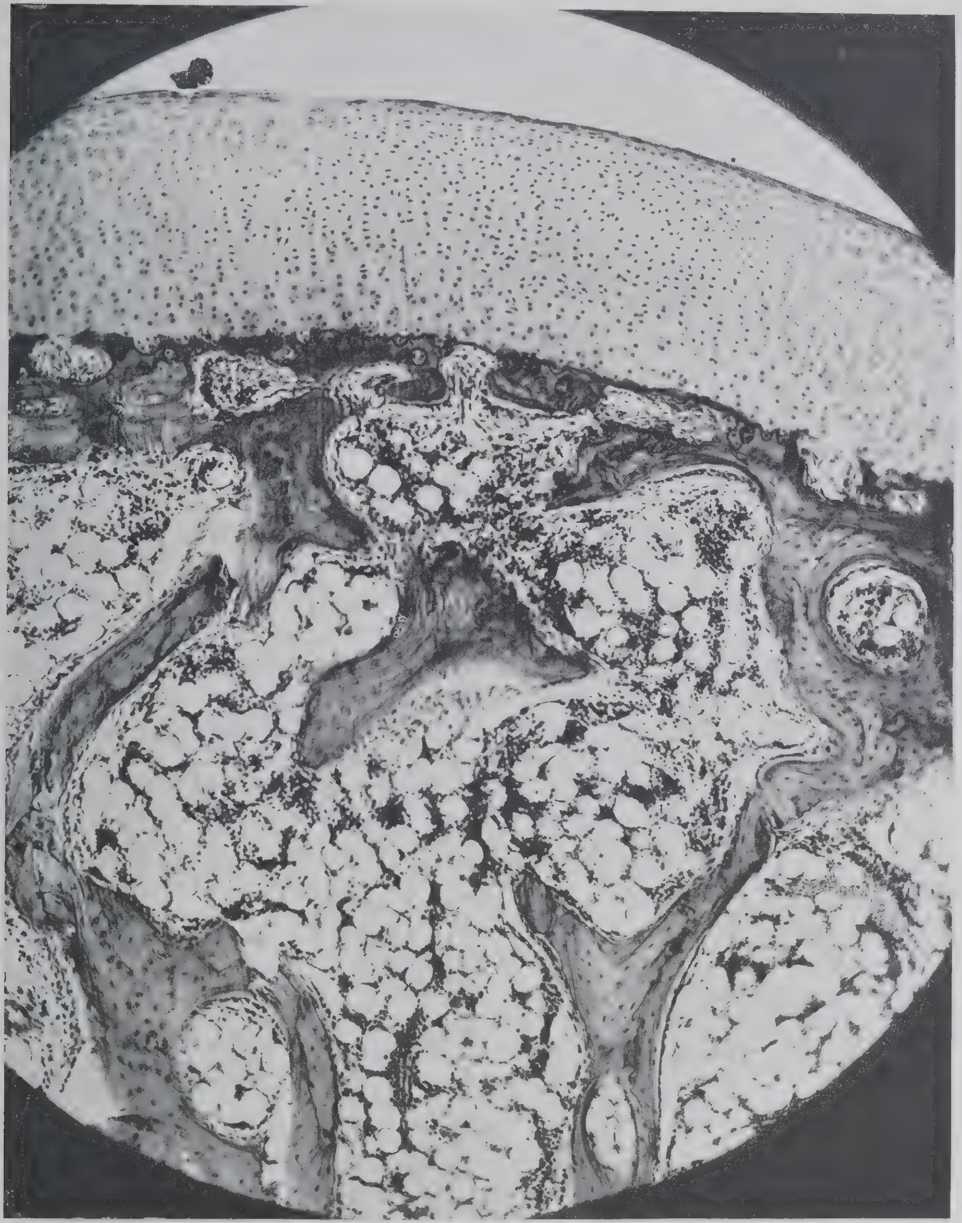


FIGURE 220. A DEGENERATIVE PROCESS IN TRABECULAE AND CORTICAL LAYER OF A RHEUMATIC JOINT.

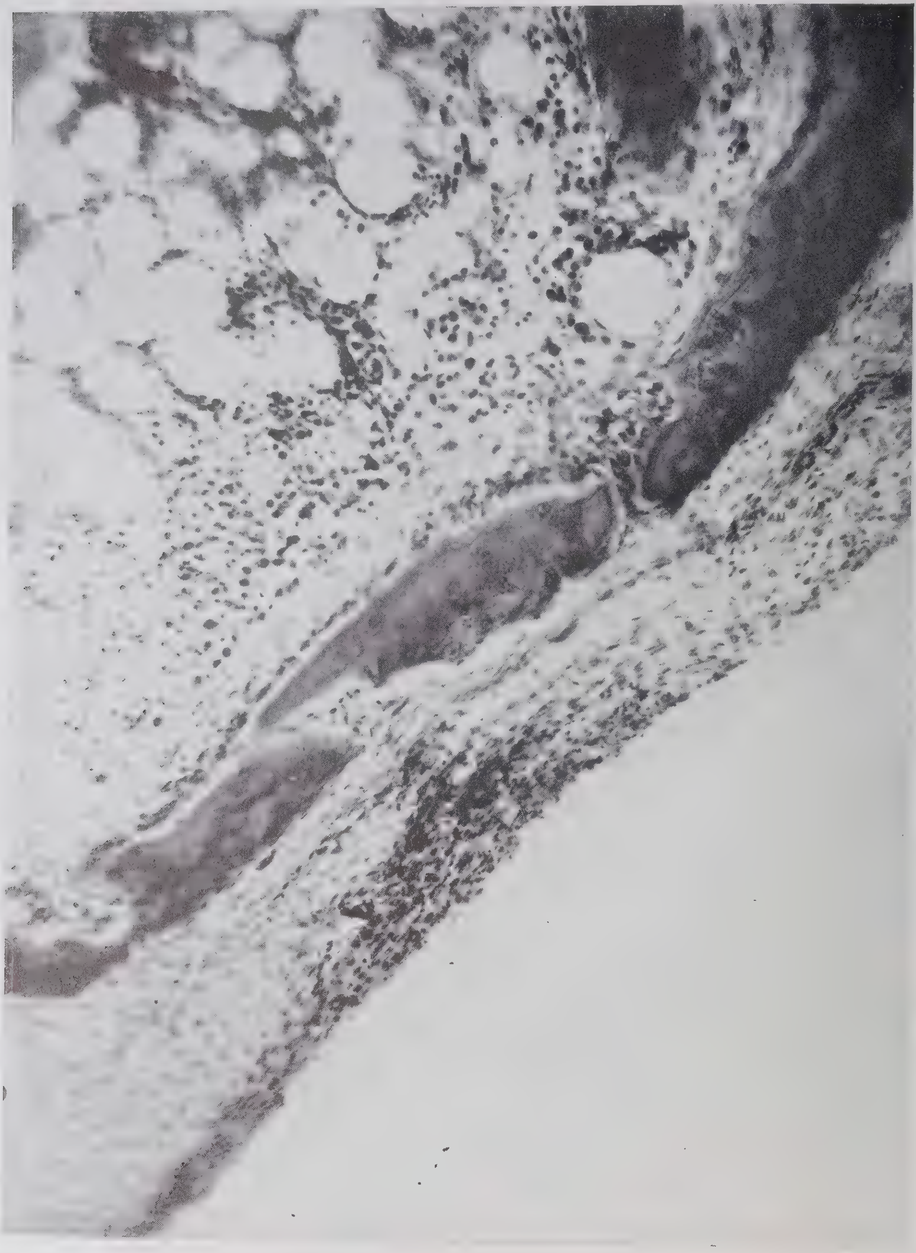


FIGURE 221. BEGINNING INFLAMMATORY PROCESS IN THE SYNOVIAL MEMBRANE.

FIGURE 222. DIPLOCOCCI SEEN IN A SMEAR FROM A RHEUMATIC JOINT.

smear. These are shown both free and phagocyted in Figure 222.

Irritations of the peridental membrane which stimulate its cells to an osteoclastic reaction may produce changes in any adjacent hard structures. Consequently the processes which attack the alveolar bone frequently attack the cementum and even the dentin of the tooth. A most striking and interesting illustration of this is shown in Figure 223, in which instance a lateral tooth was under orthodontic treatment. As shown in 223-A, there was a large metallic filling on the lingual surface. Beneath the old metallic filling there was infected caries which had not been observed. With the addition of a little pressure on the tooth, an acute pulpitis developed; and since the case involved the movement of the cuspid, which was quite entirely outside the arch, it was deemed best to extract this lateral thereby to give available space for placing the cuspid without a long tedious operation of the movement of the molars and bicuspids. This gave us a very favorable specimen for study, a condition we had been looking for. B shows the low power view of a section of this tooth; and it will be noted that on the side receiving the pressure, the cementum is almost entirely removed. Attached to this side there were areas of peridental membrane, as shown in Figure 223-B. Two of these are

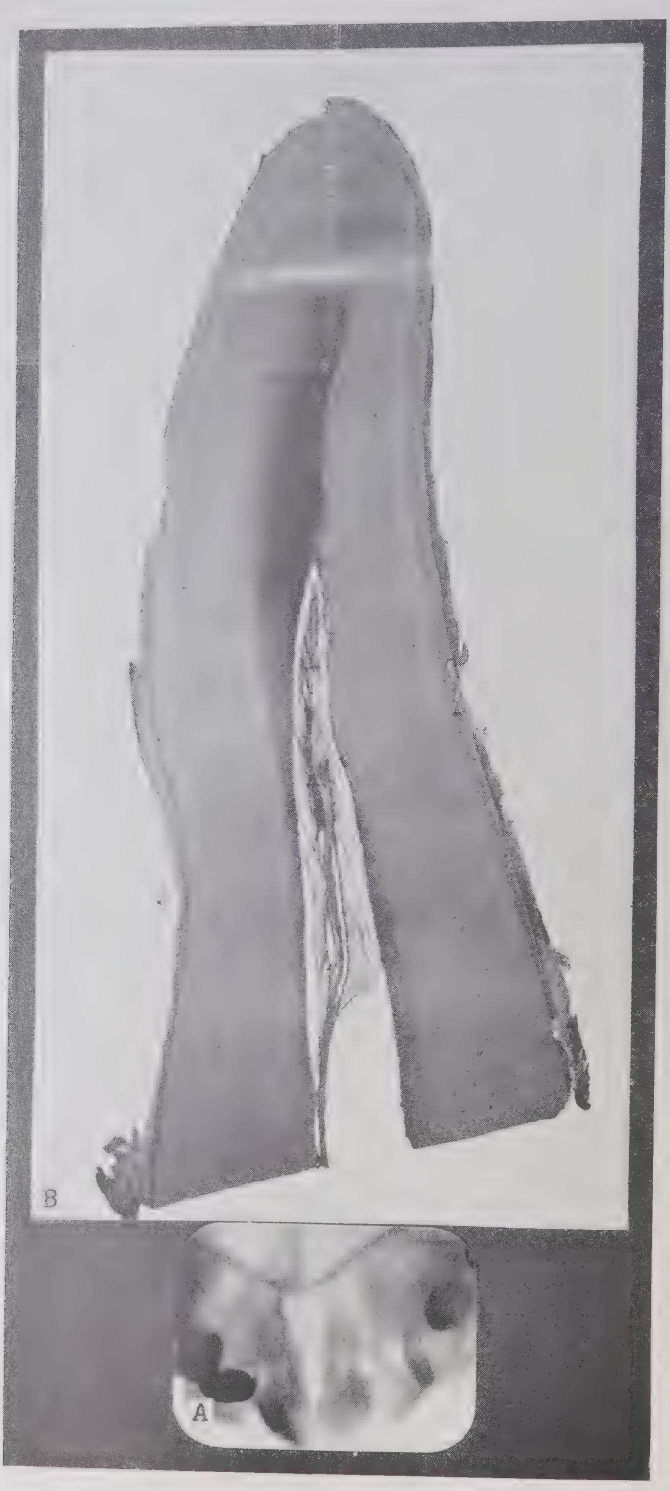


FIGURE 223. A CROSS SECTION OF A TOOTH UNDER ORTHODONTIC PRESSURE. NOTE ABSORPTION ON THE ADVANCE SIDE OF MOVEMENT.

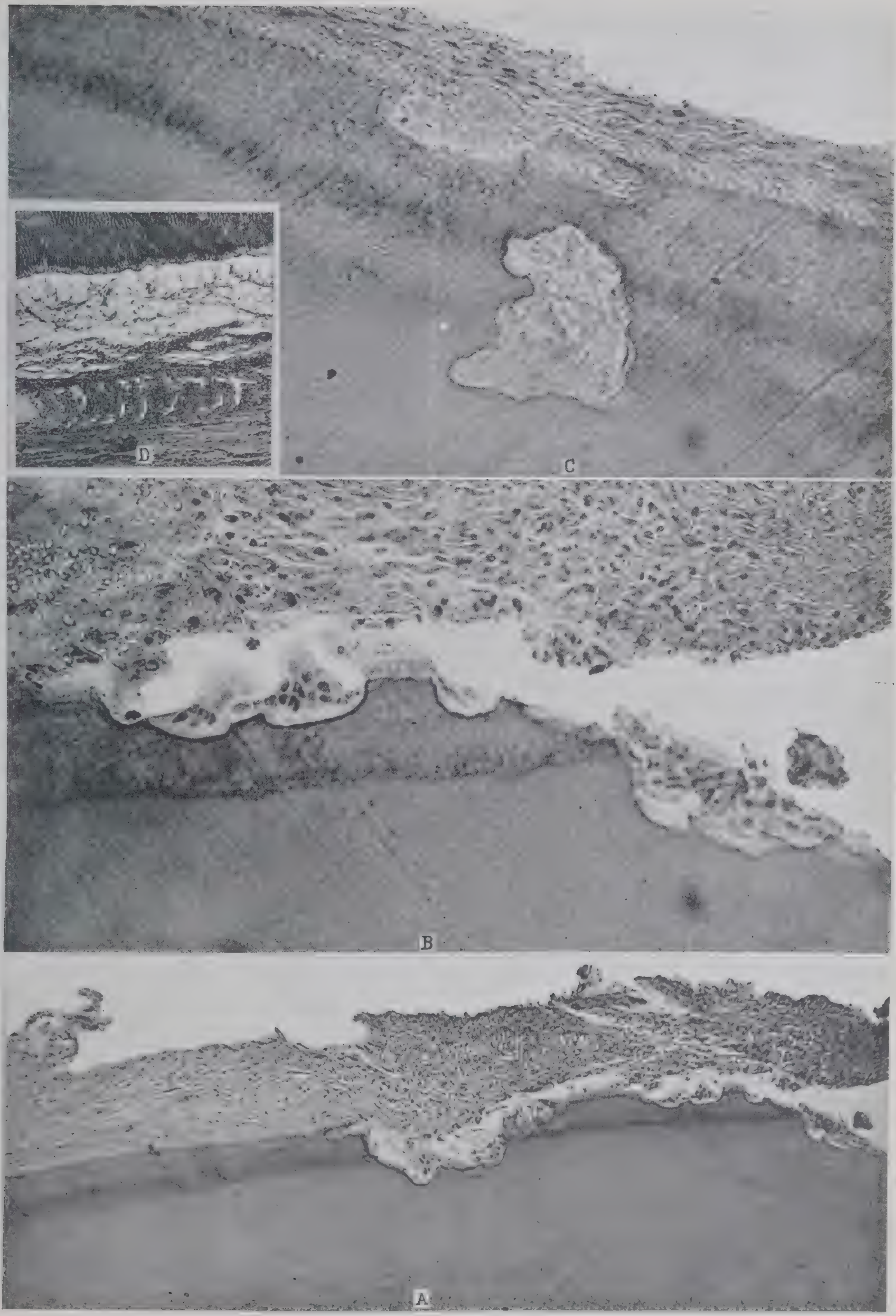


Figure 224. A, B, and C, osteoclastic activity; D, hemorrhage into pulp of tooth of previous figure.

shown in Figure 224-A and B, in which it will be observed that the cementum has been entirely removed in places and the process is proceeding into the dentin. The osteoclastic cells are clearly shown in the process of removing this structure. It is also important to note that this process has extended in some places deep into the dentin. A section across one of these burrowing excavations is shown in Figure 224-C. Either due to the toxic materials from the caries or to the mechanical trauma of the orthodontic process, or both, there was developed, as previously stated, an acute pulpitis. It is exceedingly interesting to note that there were profuse hemorrhages into the pulp tissue which, apparently, had previously been undergoing a process of fibrosis. This is shown in Figure 224-D.

When we study clinically some of our patients who have had deforming arthritis for years, we find that not only is there evidence of the most indisputable type that the dental infections have contributed directly to the development of the arthritis, but there is just as indisputable evidence that some of these individuals have had characteristic degenerative processes produced in their teeth, which were not otherwise involved, by their general rheumatic condition. In the former of these two conditions, one of the forms that the evidence takes is that individuals who have suffered for years from acute or subacute processes, have had complete and continued relief from the recurring exacerbations, and a change of their general state from one that had been getting progressively worse to one that became progressively better; and this same history had repeated itself in the same individuals by the subsequent involvement of other teeth, followed by a return of their acute processes, all tending to a return toward normal with removal of the dental infections. But note, in these cases these changes, which developed following the involvement of new teeth, were related to a primary injury to the tooth in the form of deep caries involving the pulp, which developed in the regular sequence, periapical involvement, and degeneration and irritation of the supporting structures. In the latter of these two conditions—namely, where the arthritis produces injury and degenerative processes in the teeth—we have found these degenerative changes, first in the peridental membrane, and then in the pulp, without the approach of caries or any apparent evidence such as will ordinarily be found requisite to produce a destruction or change in the dental pulp. To cite a specific case, one of the arthritic cases that I am watching very closely has in five years had six teeth come to have non-vital pulps, or definitely involved and infected pulps, without the approach of dental caries; and in every instance after the removal of these teeth, the patient experienced distinct and marked improvement. This is a matter of extreme importance, for if the teeth may become involved as a result of the systemic rheumatism, as well as be an important causative factor, it will throw an entirely new light upon our responsibility in the care of arthritic cases. But this is so important a matter that I will make it a separate study in the next chapter.

SUMMARY AND CONCLUSIONS.

Characteristic localized structural changes develop in the supporting structures of teeth when the latter carry infection within their structures. These changes are, however, determined chiefly by the host and are an expression of the reacting characteristics of the host rather than an expression of the invading bacterium.

CHAPTER XL.

DENTAL INVOLVEMENTS CAUSED BY ARTHRITIS.

PROBLEM: Can arthritic infections of the body attack and devitalize the teeth?

EXPERIMENTAL AND DISCUSSION.

It has been presumed that the teeth are only subject to the diseases which may be directly caused from the entering in and around them of infection. Some years ago I noted in my records that all the bones of patients having arthritis of a certain type tended to be more dense than normal, while other types of arthritis tended to have little condensation, and in some instances definite reduction in the calcification. By studying the maxillæ in mandibles of these patients we have found that the medullary spaces were very much smaller and the trabeculæ formed a very much larger percentage of the body of the cancellous bone in patients with arthritis. It often took the form that resembled a quite uniform condensing osteitis throughout the entire mandible or maxilla.

One of these cases I have been studying for twenty-five years. In 1901 I roentgenographed her teeth and found that a filling in an upper right bicuspid, that had been put in years previously, did not extend to the apex, and proceeded thoroughly to sterilize and correctly to root fill it, for the teaching of that time was more confident than the teaching of today, that dental infections could be readily destroyed by any one of many forms of medication, if properly applied. As shown in my roentgenogram taken in 1901, there was definite apical absorption with a concentric arrangement of the trabeculæ about the apex, which I now take to indicate a series of exacerbations and reactions with condensation on a part of the inflammatory process. After this tooth was, as I supposed, perfectly sterilized and root-filled, I had what I probably showed, as many others are doing today, what I supposed to be evidence of my remarkable skill in sterilizing this tooth and making it safe for this patient; for, as shown in B of Figure 225, the apical area of absorption filled in, and from this indisputable evidence the infection had been all destroyed, which fact was also

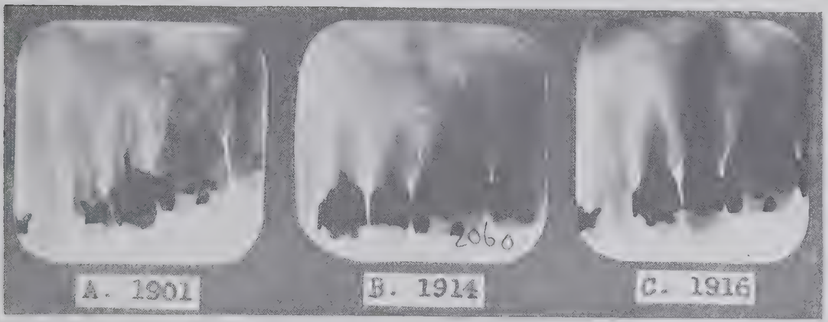


FIGURE 225. PROGRESSIVE DEVELOPMENT OF RADIOPACITY OF SECOND BICUSPID OF PATIENT WITH DEFORMING ARTHRITIS. A, IN YEAR 1901; B, 1914; C, 1916.

guaranteed by the symptom that the tooth was not in the least sore, and comfort endorsed the guarantee. But at the time I did this, this patient already had deforming arthritis following a severe attack of rheumatism, which had been so severe that her hands were already deformed and becoming rigid. Her ankles were also slightly involved. During the years from 1901 to 1916 I saw her occasionally, made dental repairs, and, as my researches progressed, I finally became very much alarmed and conscience stricken for fear the fact, that she was getting progressively and seriously worse, might be due in some part to my mistaken interpretation of the assurances of the success of my operations. I, accordingly, sent for her, at which time she was so nearly immobile that she practically had to be carried to the office. With the removal of these two teeth, with the condition as shown in Figure 225-C, she made a very definite and marked improvement.

But at the time of their removal I took great care to study her case in further detail. I undertook to remove the teeth without the possibility of the mouth infection's contaminating the roots, which was accomplished by using the actual electric cautery with which I seared the anesthetized tissue deep into the alveolar bone surrounding the necks of these teeth. Upon their extraction, I drilled into the apices and found both these bicuspids infected. (This matter of drilling into extracted teeth after sterilizing the surface, and culturing the chips has been done very many times in the last six years, and practically without exception I have found the teeth which I was testing to be infected.) But, in addition, I drilled into the bone a quarter of an inch beyond the apex and found the same strain of streptococcal infection in the bone. Three months later, under local anesthetic and actual cautery to sterilize the surface, I again drilled into the periapical bone and found it still infected with this same strain. These findings, together with the fact that this patient who had been growing progressively worse, had now become progressively better, not only put me in a new attitude regarding her teeth, but put her in a state of such positive conviction regarding the relation of her teeth to her health that, from that time to the present, she has persistently urged that I extract all her remaining teeth. My attitude has been to be ready to extract any teeth that I thought might be doing her more harm than good, but since she could only put one hand to her mouth to remove a denture and would therefore, if she got much worse, be in a position where she could not handle artificial teeth, it seemed very desirable to retain such teeth as were definitely free from involvement and not subject to the possibility of contributing to her dental condition. Since that time, as stated above, six teeth, one after another, have become involved, (as evidenced by the symptoms which I will presently recite), and have one after another been extracted, after each of which extractions she has expressed a confidence that she felt definitely better. When asked how she knew, the reason she recently gave was that she had again become able to sew, a thing that had not been possible for years.

Just here I wish to introduce a warning: Exodontists and physicians who do not have the heart rending worries of making dentures comfortable and serviceable under conditions which are so nearly impossible as to very discouraging, but where the very nutrition of the patient demands a persistent effort, will be disposed to take the evidence just cited as justifying the extraction of all the teeth for this and similar patients. I wish to stress that we have come to the time when involved teeth can be so definitely differentiated from those that are not involved, or with sufficient limit of error, that we are not justified in condemning all of the teeth for fear they may be involved. I am seeing continually, patients who are suffering more from the inconvenience and difficulties of mastication and nourishment than they did from the lesions from which their physician or dentist had sought to give them relief.

In Figure 226 I have shown in a series, A to G, the six teeth that have been extracted since the above experience, one or two a year; and some interesting and important data have been accumulated regarding their conditions. In the preceding chapter, I have

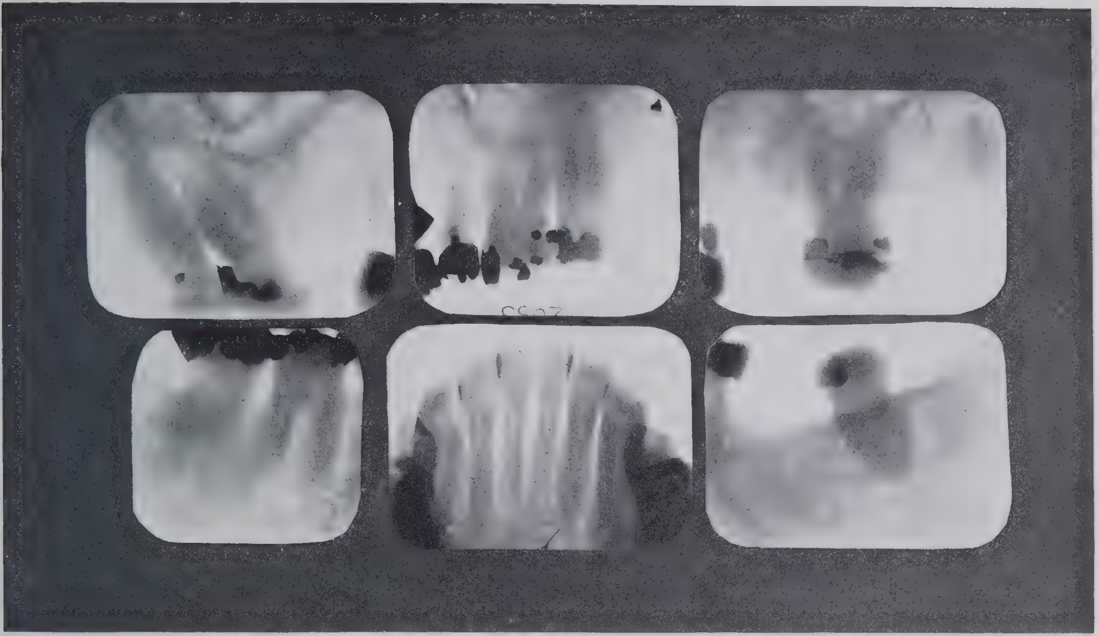


Figure 226. Six teeth which became non-vital in succession in the mouth of a patient with deforming arthritis.

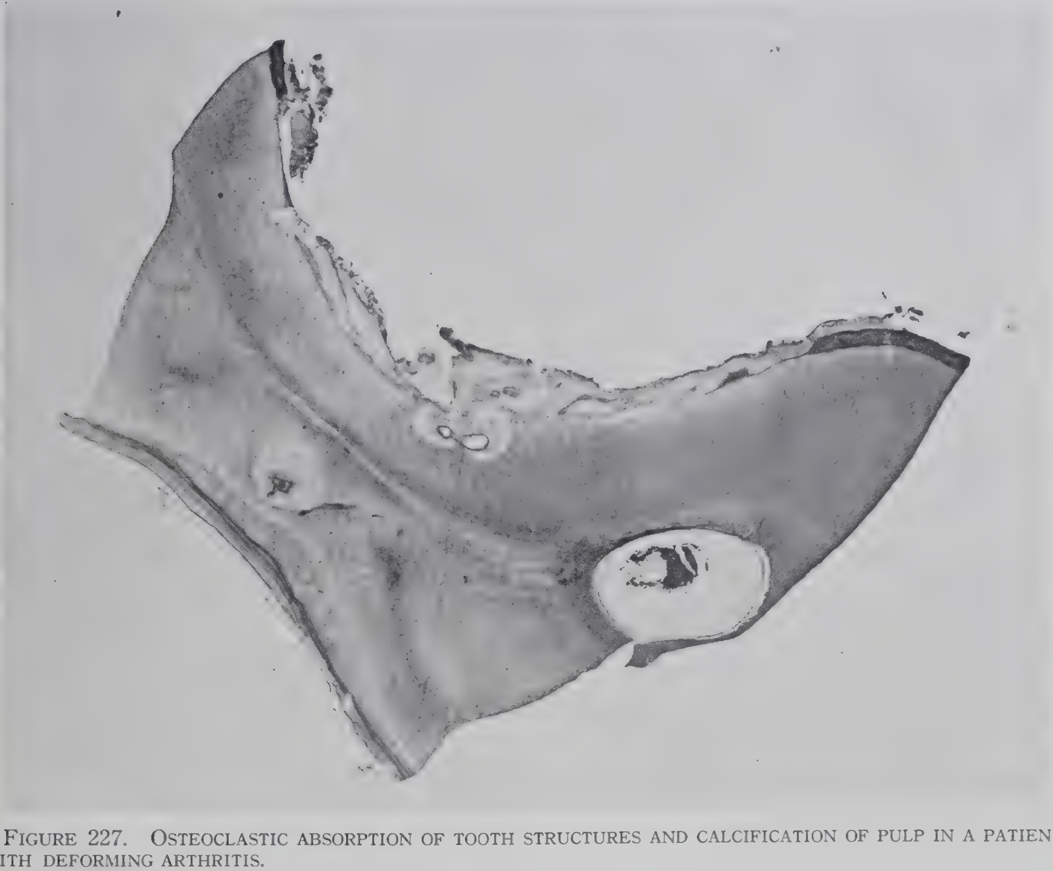


Figure 227. Osteoclastic absorption of tooth structures and calcification of pulp in a patient with deforming arthritis.

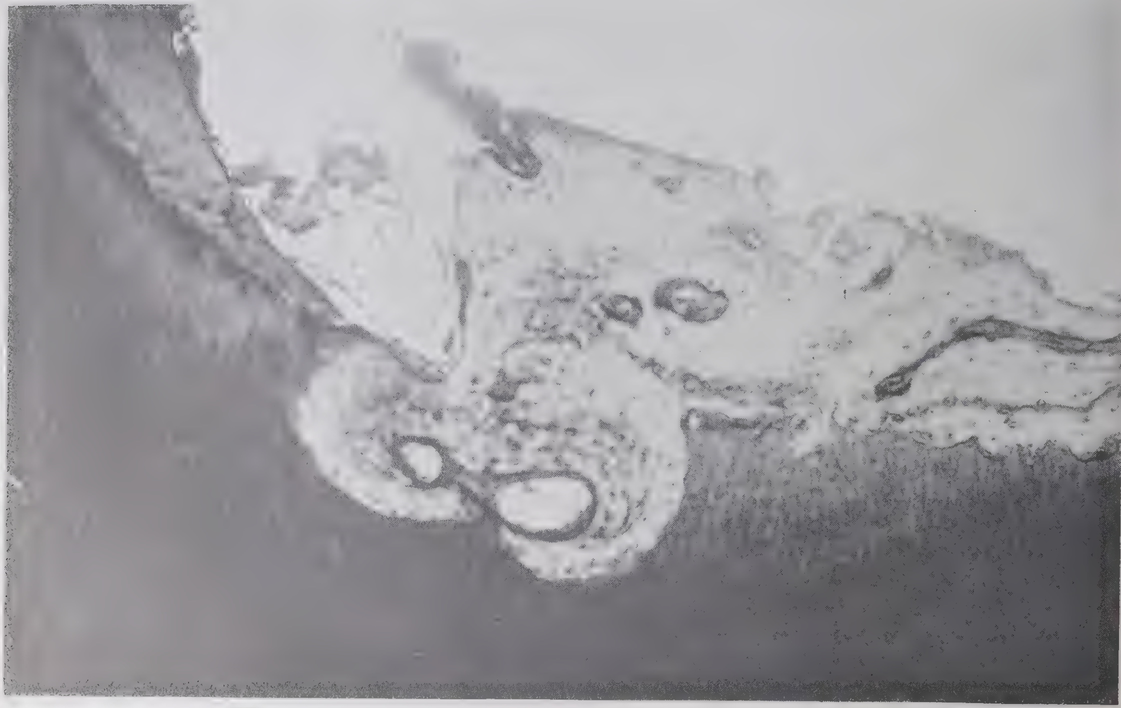


FIGURE 228. ABSORPTION OF CEMENTUM AND DENTIN AS PART OF ARTHRITIC DISEASE OF TOOTH SHOWN IN FIGURE 227.

shown in Figure 217 a histological section of the process of bone absorption, in which the giant cells are busy carrying away the bone structure. In Figures 220 and 221 I have shown some of the process of joint degeneration in the earliest stages of arthritis, and in Figures 218 and 219 I have shown illustrations of two types of rheumatic arthritis, one degenerative and the other proliferative, as evidenced by the marked depositions of the bones involved in Figure 218-B, C, and E, and the destruction and absorption of the head of femur in 219-B.

With these processes in mind, let us study the histological changes that have been taking place about the teeth of this patient as they have become involved. In Figure 227 we have a cross section of an upper left molar which had developed symptoms which made me suspicious that it was degenerating. The beginning of calcification of the pulp of one of the roots is shown. But more important for this immediate consideration is the process of absorption taking place upon the surface of the root, for it will be seen that an inflammatory irritation is in progress, which has destroyed the cementum of a considerable area and is penetrating far into the dentin. Figure 228 shows a larger view of this process, and it will be seen that this structure is highly vascularized and is

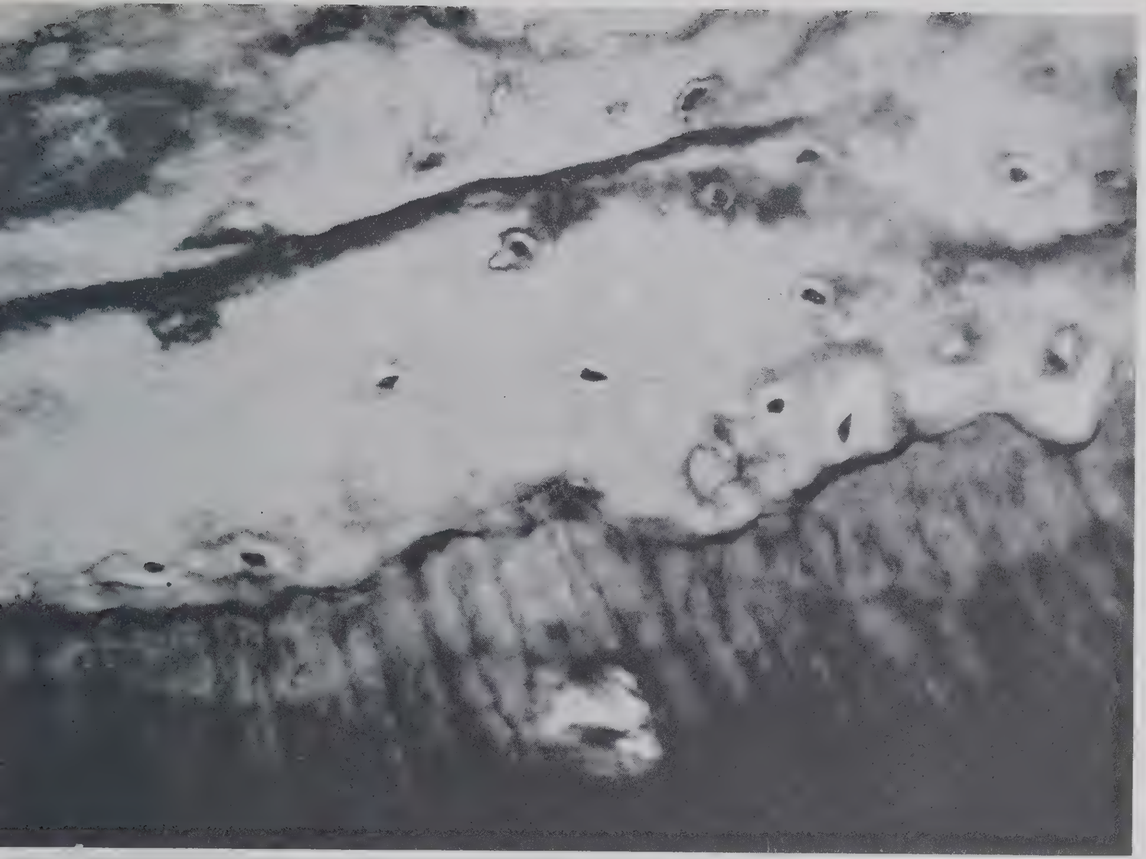


Figure 229. Osteoclastic activity, high power, of Figure 228.

abundantly filled with a special type of cells and that it is burrowing deeply into the dentin. A still higher magnification of this condition is shown in Figure 229, in which it will be seen that these giant cells are very abundant. Some are in close contact with the dentin; others are migrating. We have in this process a reaction very similar to that taking place in degenerative arthritis of joints. This is distinctly shown in Figure 230, which is a histological section of an acute inflammatory process produced in the joint of a rabbit by the inoculation of a strain producing arthritis; and it will be noted that the process is almost identical with that we have taking place about this tooth.

If we would refer again to Figure 227, we will note the beginning of decalcification of this pulp. Figure 231 shows a higher magnification of this, and it will be noted that the zones of calcification tend to develop around blood vessels and in the odontoblastic layer. The pulp tissue has largely lost its original structure. Fibrous bands are forming beneath the odontoblastic layer and around the blood vessels, and these in turn are becoming calcified. In other illustrations, we have shown lamination of pulp depositions by the successive layers becoming calcified. This process may go

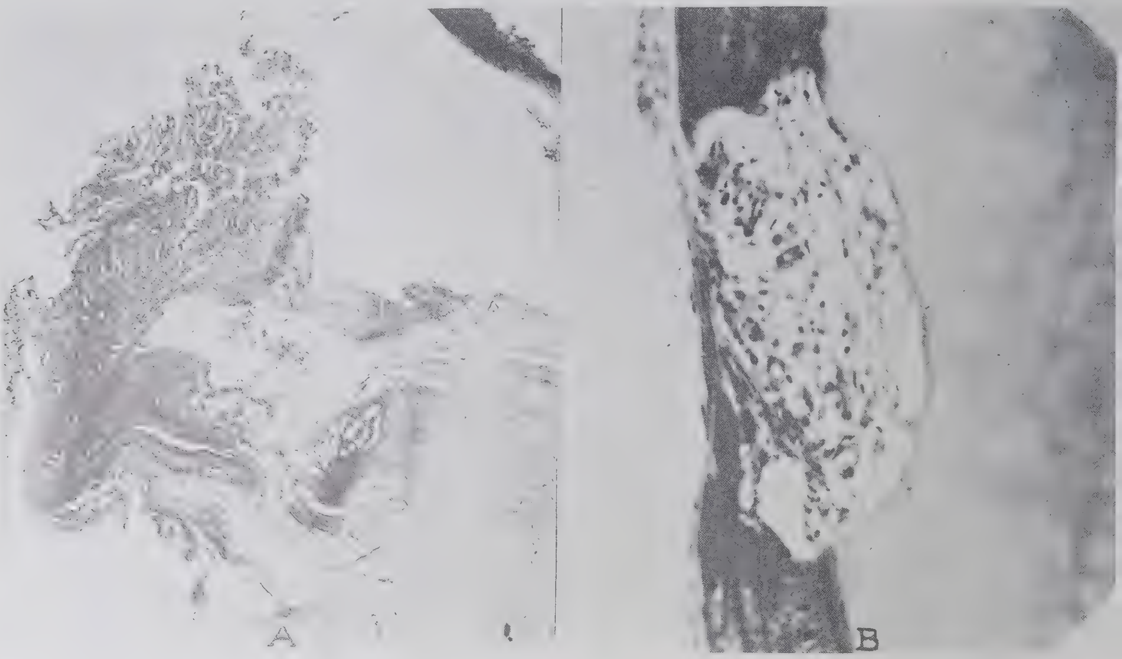


FIGURE 230. OSTEOCLASTIC REACTION PRODUCED BY RABBIT: A, IN AN ARTHRITIC JOINT; B, IN AN IMPLANTED AND ENCYSTED TOOTH.

on until the pulp has been very largely, or practically completely, obliterated by calcification. This is illustrated by one of the teeth extracted from this patient, a cross section of the root of which is shown in Figure 232. When the roots were cut from this tooth at the crown, it was found that not only were both roots completely calcified, but the entire coronale part of the pulp chamber was filled with a closely fitting casting. One huge pulp stone had apparently come to fill the entire pulp chamber. By referring to the roentgenogram of this tooth, shown in Figure 233, it will be noted that there was no evidence of root canals or of pulp chamber. This latter fact should be considered very important, as will be shown in the diagnosis of this condition.

A very important factor regarding this tooth (the upper right first molar) was the following: that notwithstanding this extreme and apparently complete calcification of the pulp, the tooth was not only hypersensitive to hot and cold, but was sensitive to irritation of the exposed dentin to instrumentation. The patient complained that she would be awakened in the night by the pain in this tooth resulting from her mouth's opening when she was asleep, and the cold air chilling the tooth would produce so violent

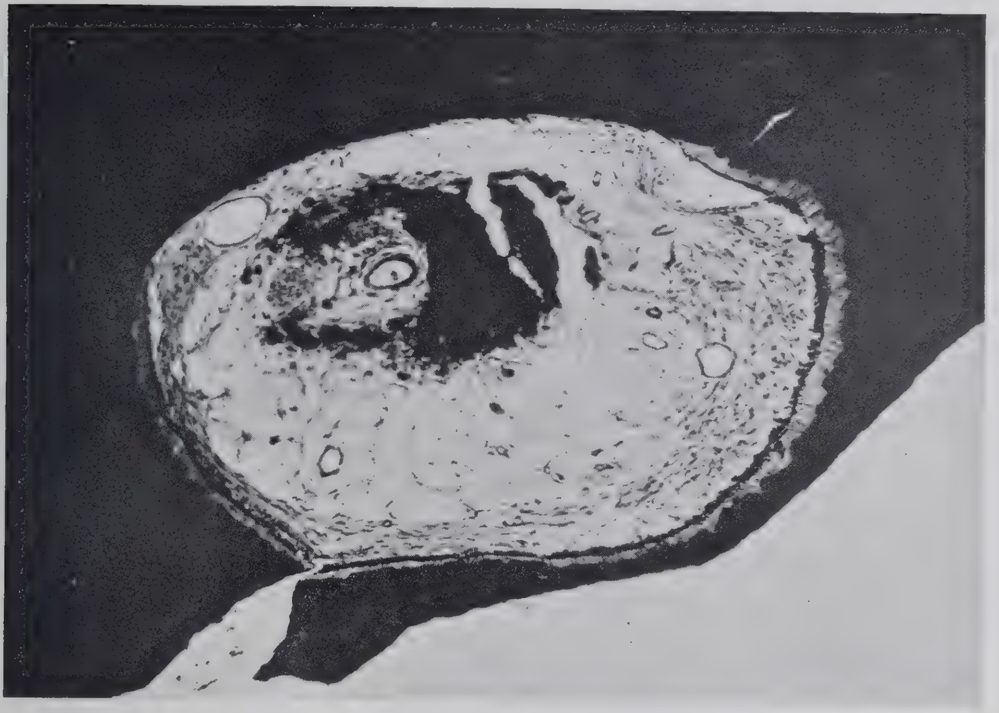


FIGURE 231. CALCIFICATIONS IN THE PULP OF TOOTH SHOWN IN FIGURE 227.

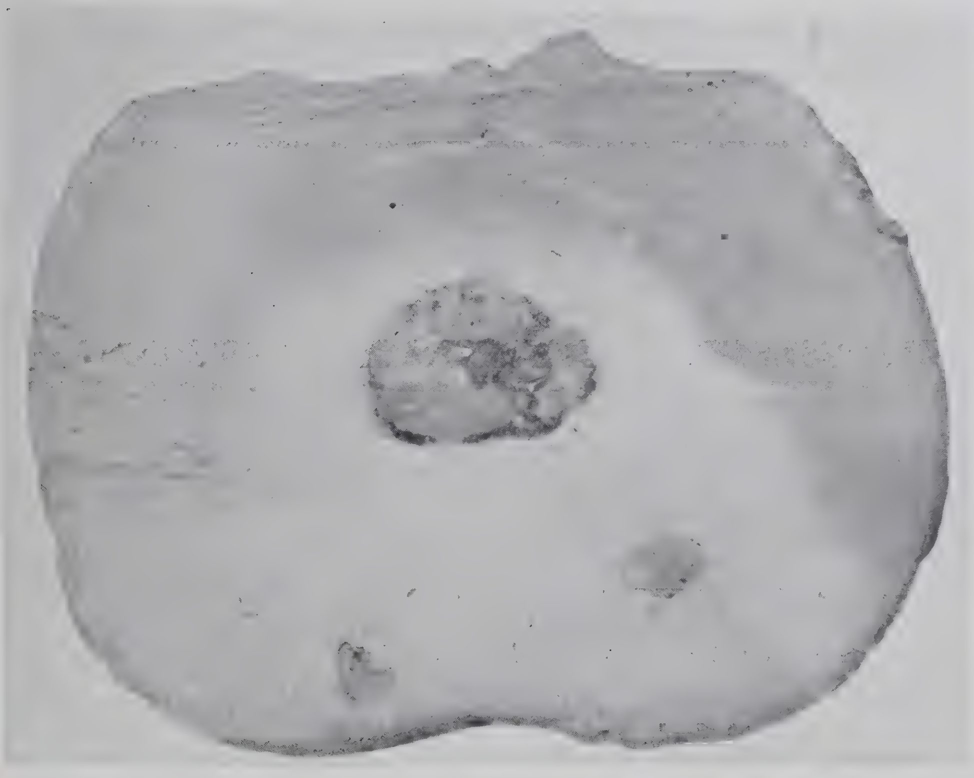


FIGURE 232. CROSS-SECTION OF A DECALCIFIED PULP FROM A PATIENT WITH ARTHRITIS.

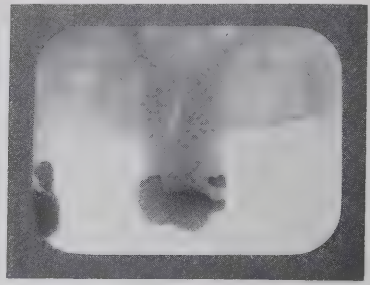


FIGURE 233. ROENTGENOGRAPHIC APPEARANCE OF TOOTH WITH COMPLETELY DECALCIFIED PULP, SHOWN IN FIGURE 232.

a toothache that it would waken her. After her mouth had been closed a sufficient length of time, the tooth would become warm and the pain would cease, all this to be repeated if she continued to sleep in a cold room, for she could lie only on her back, in which position the mouth tends so readily to open.

With regard to the matter of diagnosing these teeth, those teeth which have become involved have passed through the following progressive history. There would be symptoms of tenderness or irritability such that she would want to make pressure on them, or they would be tender to pressure, not acute as develops from pericementitis from an infected pulp. This stage was followed by one of hypersensitiveness to heat and cold. In two of the teeth where she did not heed these symptoms promptly enough, the two lower incisors, the pulps became non-vital and non-responsive to thermal change. Two or three times a year we carefully go over the remaining teeth of this patient and test each tooth in succession for normality to reaction to thermal change, to history of tenderness and the roentgenographic appearance of the pulp. On extraction, these teeth frequently show either macroscopically or microscopically on the surface of the cementum evidence of the arthritic process. This may be illustrated in low power or macroscopically by either a roughened condition of the cementum or the attachment to the cementum of little fibres by the frayed ends of the frayed attachments of the supporting fibres which have not torn loose from the tooth but have been broken midway, one end remaining attached to the alveolus, and the other attached to the cementum. Another condition which frequently occurs is shown in Figure 234, in which it will be seen on the mesiobuccal root that there is at one point a deep pitting of the cementum and dentin by an absorption process, and close by a nodule of proliferative deposition of osteoid tissue upon the cementum.

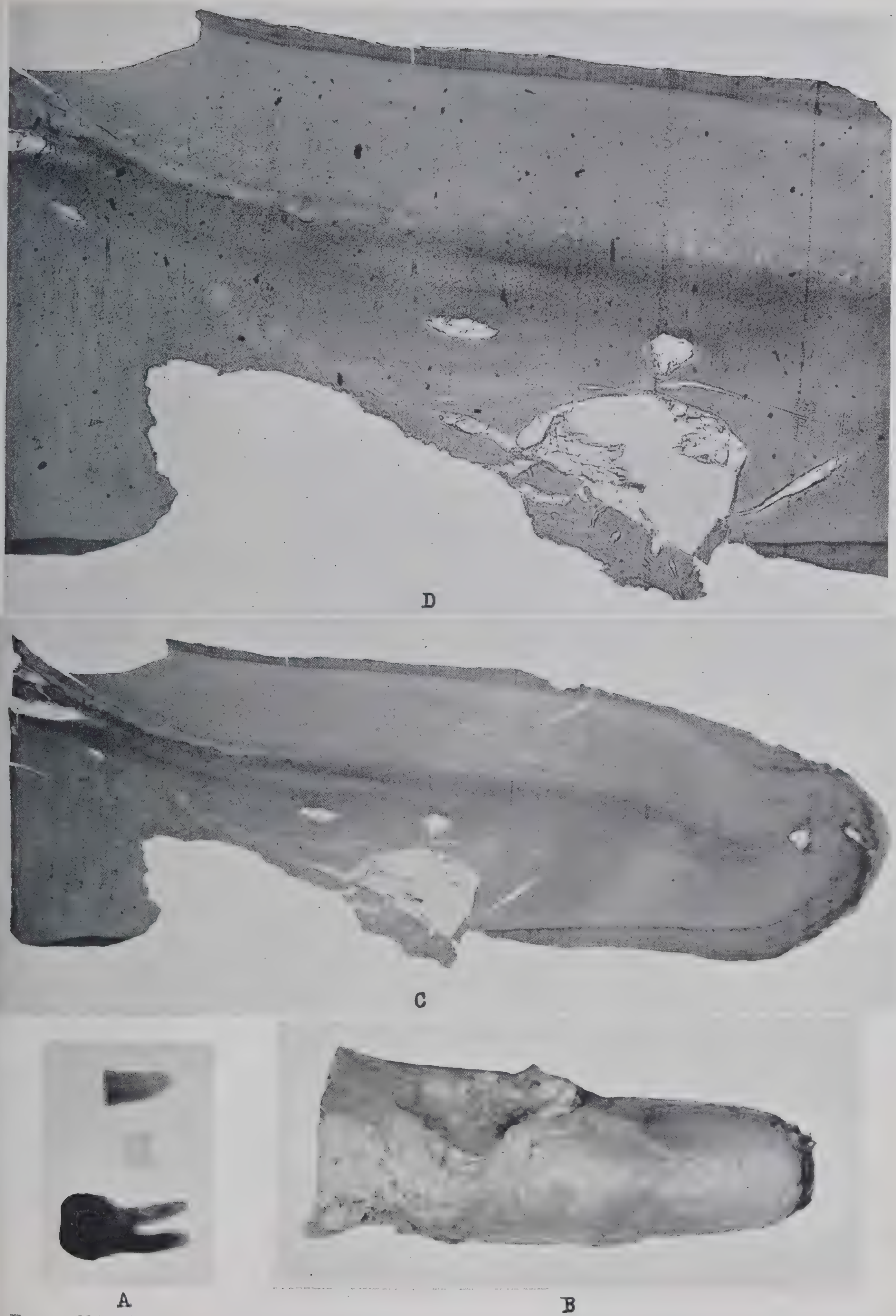


Figure 234. Arthritic changes in external surfaces of tooth with calcified pulp from arthritic patient.

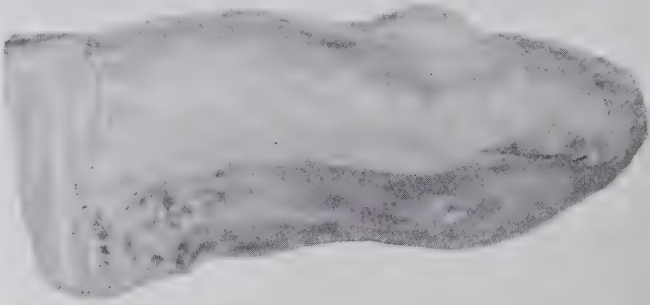


FIGURE 235. ARTHRITIC HYPERTROPHIC NODULE ON ROOT.

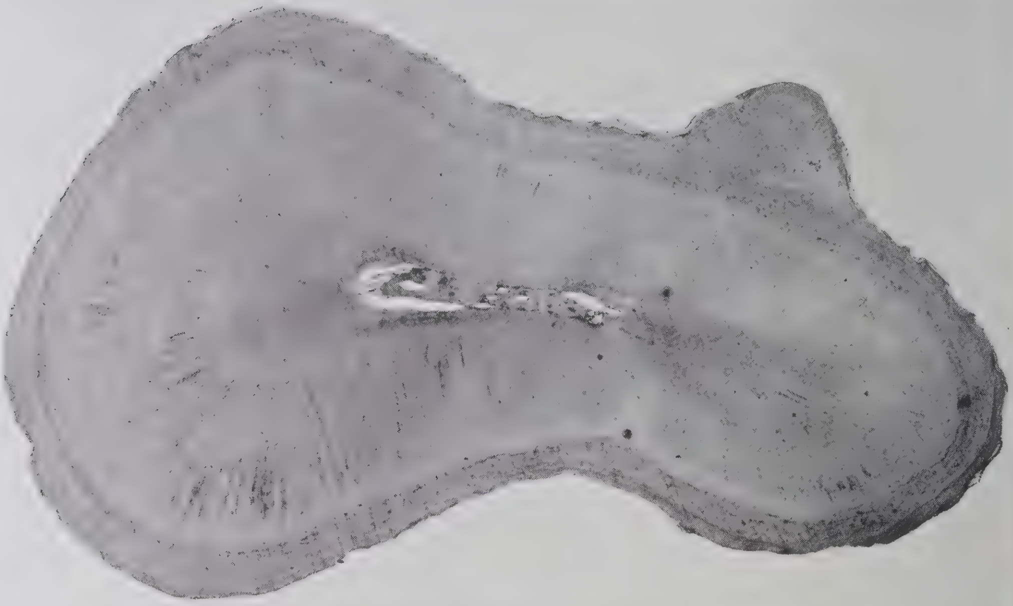


FIGURE 236. CROSS-SECTION OF HYPERTROPHIC NODULE, SHOWN IN FIGURE 235.

The distobuccal root of this same tooth had even a larger arthritic nodule built upon it, shown in Figures 235 and 236. The mesiobuccal root is shown in the cut in Figure 234. A shows roentgenograms of the two buccal roots of the extracted tooth and separately of the palatal root and of a small section cut from the palatal root to illustrate how completely the pulp chamber was calcified. B shows this deeply burrowed pit with the built up nodule of osteoid tissue. C and D show these two structures in

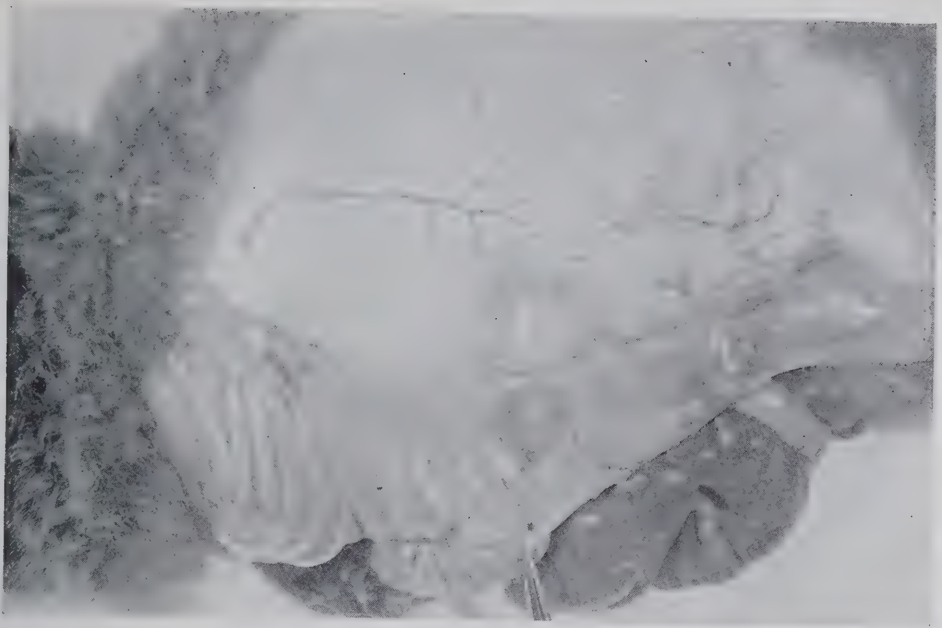


Figure 237. Skin lesion of rabbit which lost 28 per cent in weight in twenty-two days, from implantation of calcified root from arthritic patient.

cross section and higher magnifications, and it is of interest to note that the nodule is bridged over an open space, or, as it were, a cavern in the dentin with two other caverns shown deeper in the dentin.

When we remember that this tooth was not only responsive to thermal changes but was really hypersensitive and painful, showing a clearly exalted vital response, we would naturally not look upon it as being infected structure. The palatal root, therefore, when it was cut from the freshly extracted tooth, was immediately planted beneath the skin of a rabbit to determine whether it was an infected structure capable of doing the animal injury. A section of the tooth was also cultured. The rabbit shown in Figure 237, under the skin of which was planted the palatal root of the tooth we have been reviewing, died in twenty-two days, having lost 295 grams, or 28 per cent of its weight, or nearly 1½ per cent per day.

Returning to the discussion and study of the pathology of the pulp, some very interesting features had developed. As stated previously, not only was the pulp tissue of the roots entirely calcified, but also the bulbous portion. High power magnifications of this pulp tissue are shown in Figure 238. In A will be seen channels through which the blood vessels passed, and around which the calcifications developed. In B will be seen what appears very

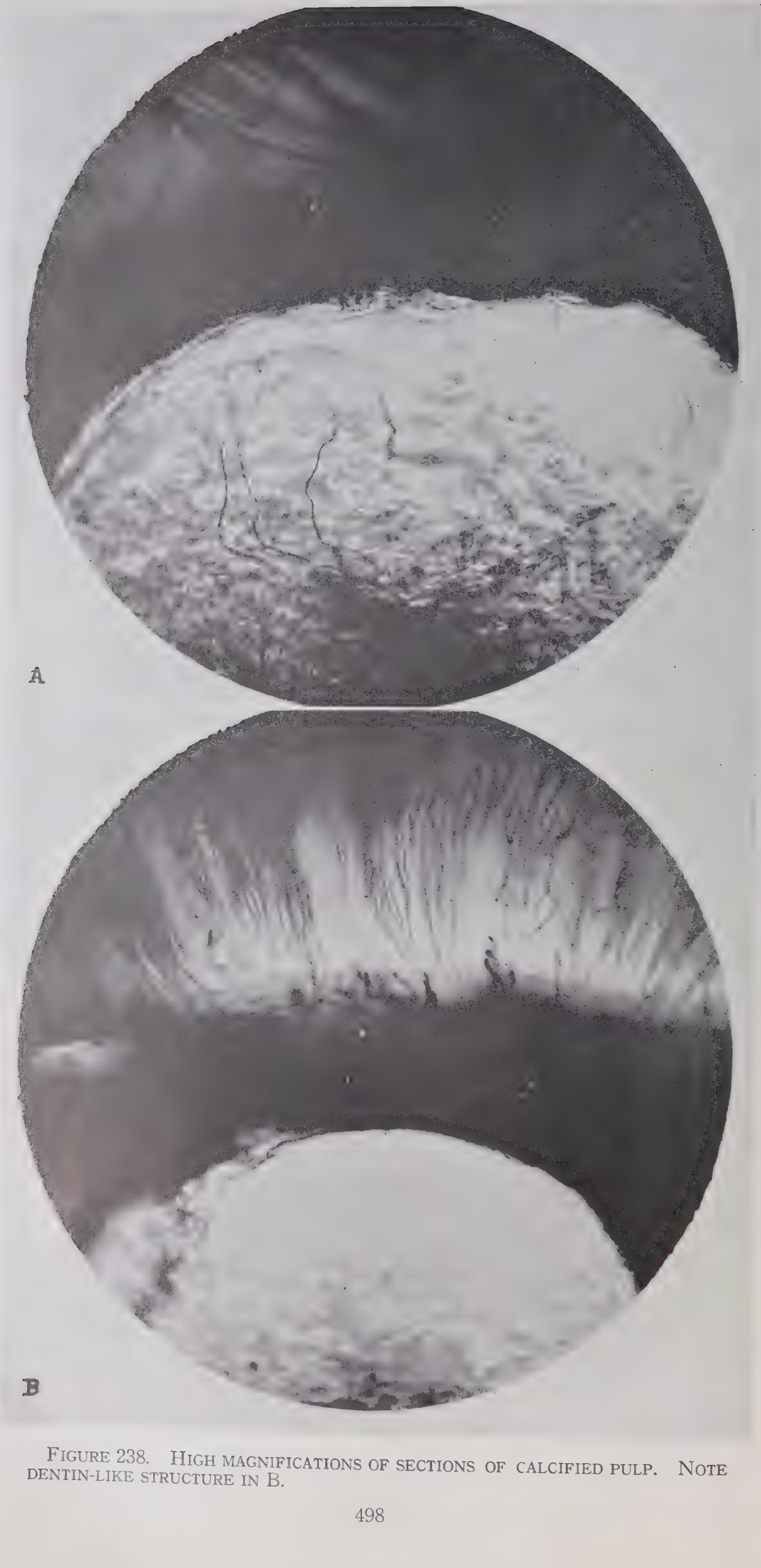


Figure 238. High magnifications of sections of calcified pulp. Note dentin-like structure in B.

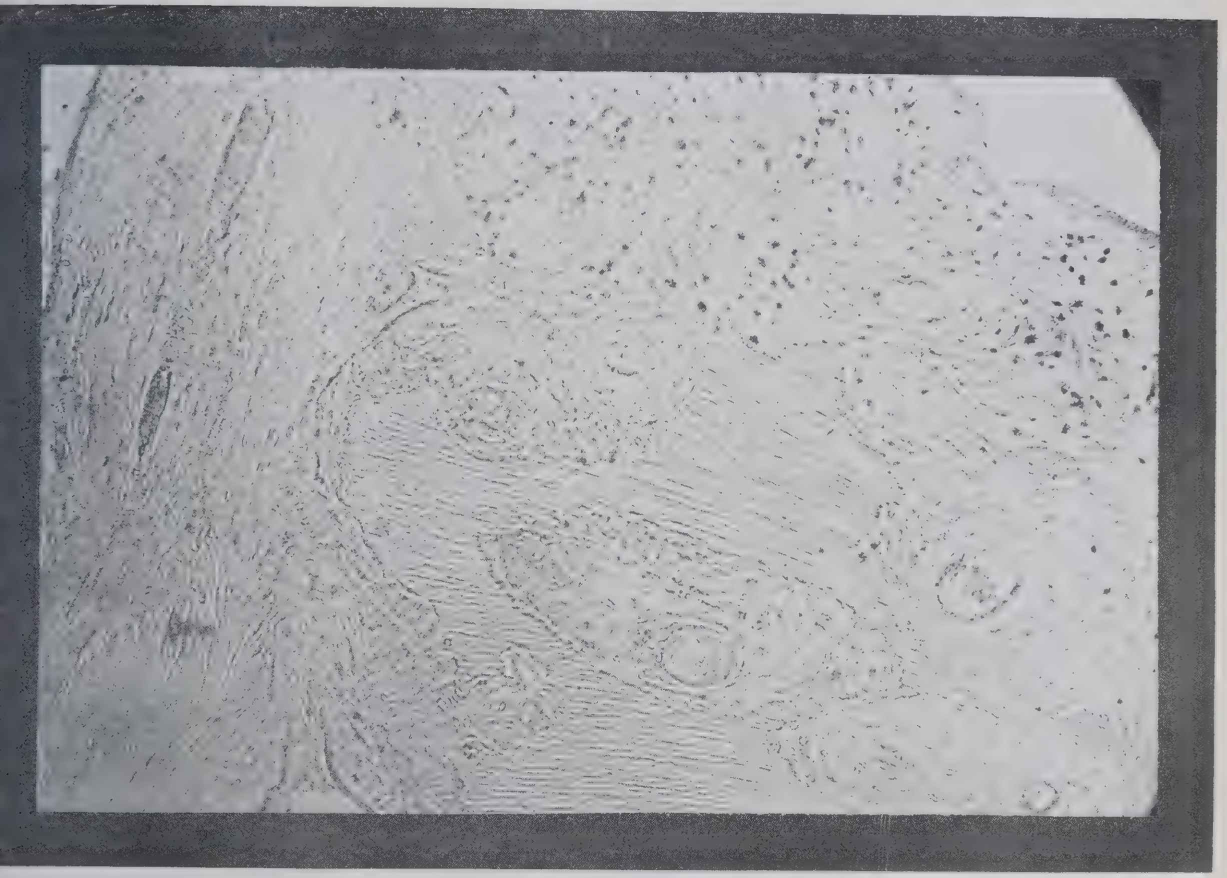


FIGURE 239. SECTION OF ALVEOLAR BONE FUSED INTO A ROOT FOLLOWING AN INFLAMMATORY REACTION.

similar to dental tubuli. But these are not in dentin; they are in this osteoid structure radiating from one of these blood vessel chambers which is shown in the lower part of the field. They do not, in this view show an intercommunicating system of connecting channels, each appearing to be dependent throughout its course. We have frequently found these in calcified pulps, and it is not impossible that they are in some way related to, either in origin or in structural type, the dentinal fibres of the odontoblasts.

It frequently occurs that this degenerative process subsides, or there is a reversal so that an absorption process is transferred into a proliferative one, and this same tissue, which up to the time of the change in systemic conditions was engaged in the tearing down of osseous and dental structures, proceeds to fill up the chambers it has burrowed out with a new structure. Of course, it cannot reconstruct dentin or cementum, not having either odontoblasts or cementoblasts; but it does have osteoblasts. It, accordingly, builds an osteoid structure, sometimes with an haversian system very closely resembling true bone. This constitutes what we have discussed as a condition of ankylosis. This is typically illustrated in Figure 239, in which instance, when I extracted the tooth, I found it necessary to chisel off every little piece, there being no clearly defined zone of cleavage between the tooth structure and the alveolus.

SUMMARY AND CONCLUSIONS.

(1) It will be seen from these data that a systemic involvement of multiple arthritis may, while attacking various joints of the body, also attack those of the joints of the teeth; and, further, that this process of inflammation with degenerative and proliferative processes may cause the involvement and ultimate death of the pulp.

(2) The involvement of these teeth as a result of the progressive systemic arthritis may in turn, and doubtless frequently, if not generally, does aggravate the general condition, for the tooth structure, when it becomes infected, is even less capable of vascularization and therefore less amenable to the processes of defense, than is bone. This stresses the very great importance that, individuals having deforming arthritis, shall have most careful dental inspection and care, and also, since it is one of the most horrible of living deaths, every effort should be made to prevent the beginning of that process; and since the evidence is so overwhelmingly that the initial infection frequently, if not generally, comes from the teeth, helpless humanity deserves pity until the powers that be shall make a worthy effort to find the means that will prevent this needless catastrophe in so many lives.

CHAPTER XLI.

VARIATIONS IN THE DEFENSIVE FACTORS OF THE BLOOD.

PROBLEM: Is there a difference in the defensive factors of the blood of susceptible and non-susceptible individuals to systemic involvements from dental infections?

In the preceding chapters, the data secured from the researches seemed to demonstrate the following:

In Chapter 3 we found that the same dental infection expresses itself quite differently, locally, in the supporting structures about the teeth in different individuals.

In Chapter 4 there is a very marked variation in the susceptibility to systemic involvement of different individuals, which susceptibility tends to be a family characteristic.

In Chapter 5 we found that these characteristics of both the local and systemic expressions are definitely related each to the other.

In Chapter 20 on Blood Calcium we found a definite relationship between the calcium content of the blood in different types of individuals, which had been grouped in accordance both with their type of local oral pathology and systemic susceptibility.

In various other chapters we found characterizations and relationships which were distinct, as, for example, the relationship to dental caries, periodontoclasia, rarefying and condensing osteitis, etc., etc.

In Chapter 38 the evidence seemed to demonstrate that the so-called dental granuloma is a physiologically acting tissue and not necessarily a degenerative type of tissue, though it may become such with a loss of function of that tissue; and that tissue, when taken from an individual with high defense, as judged from the fact that he was not having any apparent systemic expression from involved dental infections, would, when placed on or in infected culture media, show a marked inhibitive power on bacterial growth as well as produce a bacteriolysis.

In Chapter 20 we found that when an infected tooth is placed

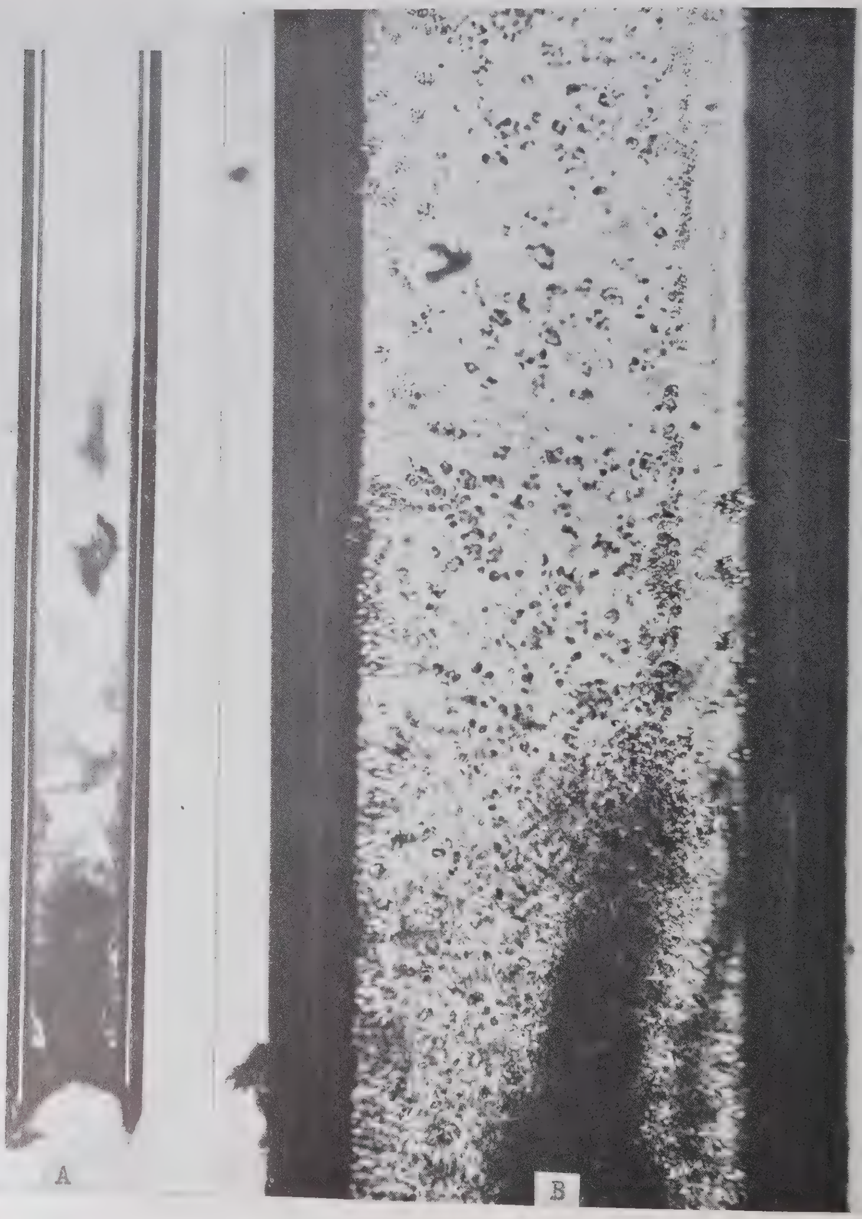


FIGURE 240. THE MIGRATION OF LEUCOCYTES INTO A GLASS TUBE, A CHEMOTACTIC REACTION WITH TOXIN.

beneath the skin of a rabbit, either the rabbit builds such a defensive membrane (in which case it is not seriously injured, or at least not promptly so), or else the rabbit's defense is rapidly lowered and it dies in a few days; and in that chapter as in preceding chapters, we found that the placing of such a tooth under the rabbit's skin produced changes in the rabbit's blood, particularly in the blood calcium, and that its prostration was largely in direct proportion to depression of the ionic calcium and the production of a pathologically combined calcium.

In Chapter 20 we found that the placing of an infected tooth in the blood serum of a patient or animal tended to reduce the ionic calcium of the serum and produce a pathologically combined calcium, and that this condition was apparently identical, whether it developed *in vitro* or *in vivo*.

If, then, the dental infection acts directly upon the defensive forces of the circulating blood, it should be possible to measure and determine these, or at least it would be of very great advantage if this can be done. To determine this, we have made the following special studies. For some time we have been studying the action of the leucocytes in the presence of various types of irritants and chemicals. It is most significant, as has been shown by others, that when a capillary glass tube containing bacteria, dead or alive, is placed beneath the skin of a rabbit, the leucocytes tend to be attracted by chemotaxis to these bacterial products and migrate rather rapidly into the glass tube. Such a condition is shown in Figure 240. In order to determine the depressing effect on the quality of chemotaxis, I have placed tubes containing cultures grown from dental infections beneath the skins of normal rabbits and have noted the distance into the tubes that the leucocytes would travel in a given time. It was found that the leucocytes migrated in large numbers to a considerable distance within the tube. One end of the tube was sealed, the open end filled with the infected culture media being in direct contact with the subcutaneous tissue as the end of the tube was slipped under the skin. When a similar tube was placed under the skin of a rabbit, into which a tooth had been planted a few days previously and for which the rabbit had sufficient defense to build an encapsulation without the production of pus or evidence of other local irritation, it was found that the tube placed not within, but in the vicinity of this cyst, had a very much less profuse migration of the leucocytes than did the normal rabbit. When we placed a tube under the skin of a rabbit which was not showing such good reaction to the tooth, for pus was developing and the animal was rapidly losing in weight, the tooth having been planted several days previously, it was found that the organisms did not penetrate so far nor so rapidly as in the normal tissue.

When we undertake to relate these data—namely, that the defense of the rabbits is not only measurable in quantitative terms by a study of the chemistry of the blood, but in the physical expressions of the leucocytes themselves—we find what seems to be a very direct placing of the responsibility for a large part of the mechanism of defense upon the leucocytes. In order to study this more exactly, I have made the following important experiments: The blood has been taken from normal animals and humans and its power to kill streptococci taken from teeth determined both with regard to quantity of organisms and the time necessary to destroy them, by placing the live organisms of a known number in the freshly drawn blood, with or without defibrination, for different periods of time, varying from one minute to sixty minutes; and since the number of live organisms was known with quite close approximation to exactness by counting and carefully measured diminutions, it became possible to test not only the capacity of the blood for reacting in the devitalizing of the live organisms, but to establish the rapidity of this process. It has been most striking and unexpected to find that the blood of normal healthy animals and normal individuals with a high defense will not only kill these organisms in very large numbers, but that it will do so in one minute's time, for the difference between the effect of leaving the organisms one hour or ten minutes leaves so little advantage in favor of the longer time that nearly the maximum devitalizing effect has occurred in ten minutes, and, indeed, in many bloods this process is almost as efficient in one minute as in one hour. Contrary to our expectation and the current teaching regarding the mechanisms of defense, which have provided that the leucocytes engulf and phagocyte the bacteria, we have found that in this devitalizing process very few of the organisms, or at least a very small percentage, have been engulfed; by far the great majority have been devitalized; and if the blood stains are not examined within a few minutes, the

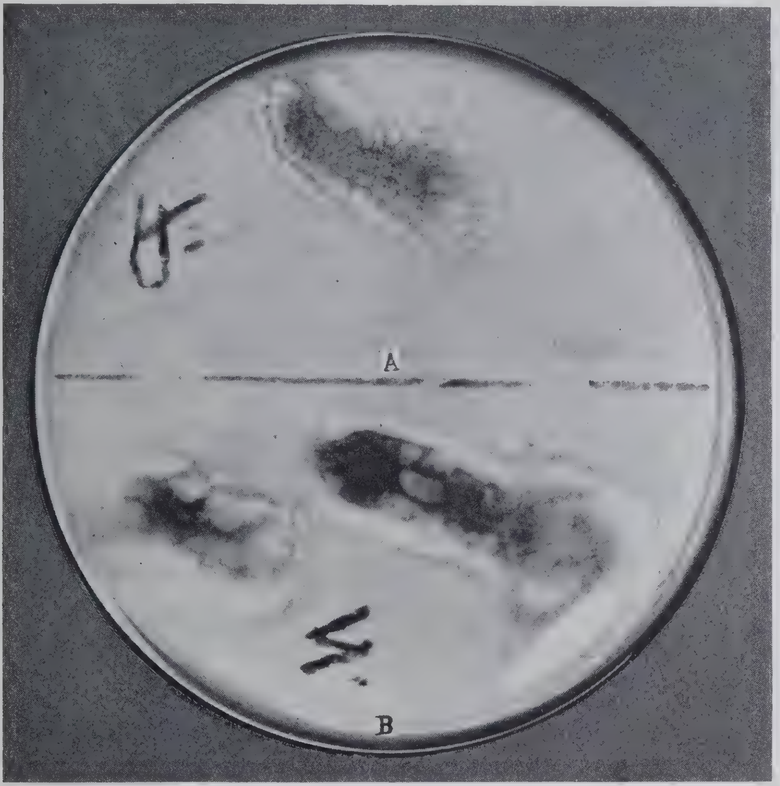


FIGURE 241. A COMPARISON OF A DROP OF BLOOD FROM A DEFECTIVE PATIENT—A, WITH A NORMAL PATIENT—B. NOTE THE CLEAR ZONE IN B, INHIBITING BACTERIAL GROWTH.

organisms will not only be devitalized, but will be digested by special enzymes provided by the blood.

Before taking up a detailed study of the relation of time and the different bloods in this devitalizing process, I wish to review experiments made by placing drops of various bloods on infected agar plates. Figure 241-A shows one drop of blood taken from a patient with a chronically low defense to streptococcal infection, suffering from xerostomia and rheumatism, and two drops of my blood in B. It will be noted that the organisms not only do not grow in or under the drops of my blood, but there is a zone for a considerable distance around my blood where this inhibition has been complete; whereas, in this patient's blood the zone is very diffuse and but slightly marked, and the organisms are growing under and over the blood. There is clearly a very great difference in the bactericidal property of these two individuals.

Important new data have been added to the available knowledge regarding the defensive factors of the blood by Sir Almroth

Wright. In the bibliography I have given references to several of his contributions. His original work on the determination of the opsonic index of the leucocytes started a new interest in these structures. During the war he made important observations regarding the defensive factors which are localized in individual wounds, such, for example, as the finding, that some wounds of a given patient had not only rid themselves of infection, but would destroy organisms that were abundant in another wound of the same patient when the dressing from the latter wound was placed on the healing wound, thus showing that the defensive factor was in part, at least, a local tissue reaction quality.

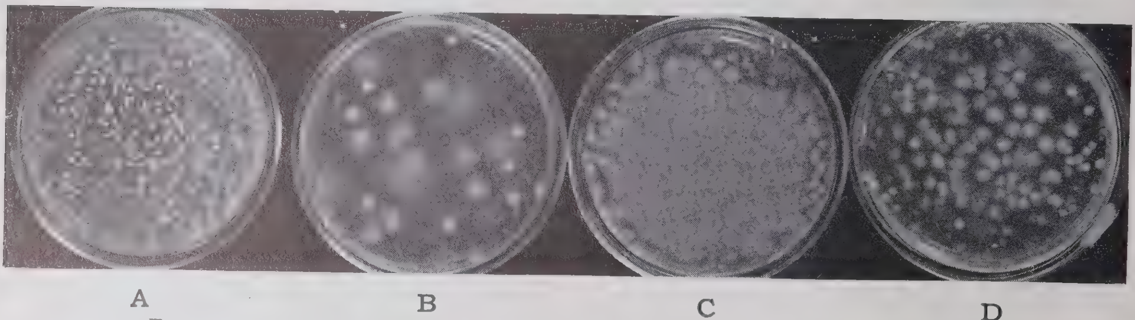


FIGURE 242. STUDIES OF BACTERICIDAL PROPERTY OF BLOOD, ONE MINUTE EXPOSURE.

In order to establish more exactly this quality of defense of different groups, I have made an extended series of platings, in which I have used the blood of the patients under study, in comparison with normal controls, to establish, if possible, the nature of the variations. In Figure 242 will be seen four Petri dishes. A is a control and contains approximately five hundred organisms placed in the agar of the Petri dish. B shows the result of taking a cubic centimeter of blood from a normal rabbit and placing these living organisms in this normal rabbit's blood for one minute. The infected blood was then placed in the agar, and it will be noted that the five hundred organisms were reduced to about fifty. A similar quantity of the counted culture was placed in a similar quantity of blood of a rabbit that had been infected by placing a tooth under its skin, shown in C. It will be noted that a large number of colonies grew out, that the infected rabbit was not able to devitalize as many of the bacteria in one minute's time as did the normal rabbit. D shows the effect of taking some of the blood from a patient whose defense has been lowered and who was suffering from rheumatic symptoms. It will be noted that while he killed more of the organisms than did the infected rabbit, he did not kill nearly so many as did the normal rabbit.

When, however, we compare the effect of using a large number of organisms instead of five hundred, even though the organisms are exposed to the blood for sixty minutes, we find a very different reaction. The result of this is shown in Figure 243. The controls, shown in A-1 and A-2, show respectively five thousand and fifty thousand organisms in the agar plates. The normal rabbit was able to kill nearly all of the five thousand and a very large percentage of the fifty thousand, as shown in B-1 and B-2. The infected rabbit did not do so well as the normal rabbit, but showed a good reacting power. (See C-1 and C-2.) The rheumatic patient, however, did not do nearly as well as either the normal or the infected rabbit, shown in D-1 and D-2.

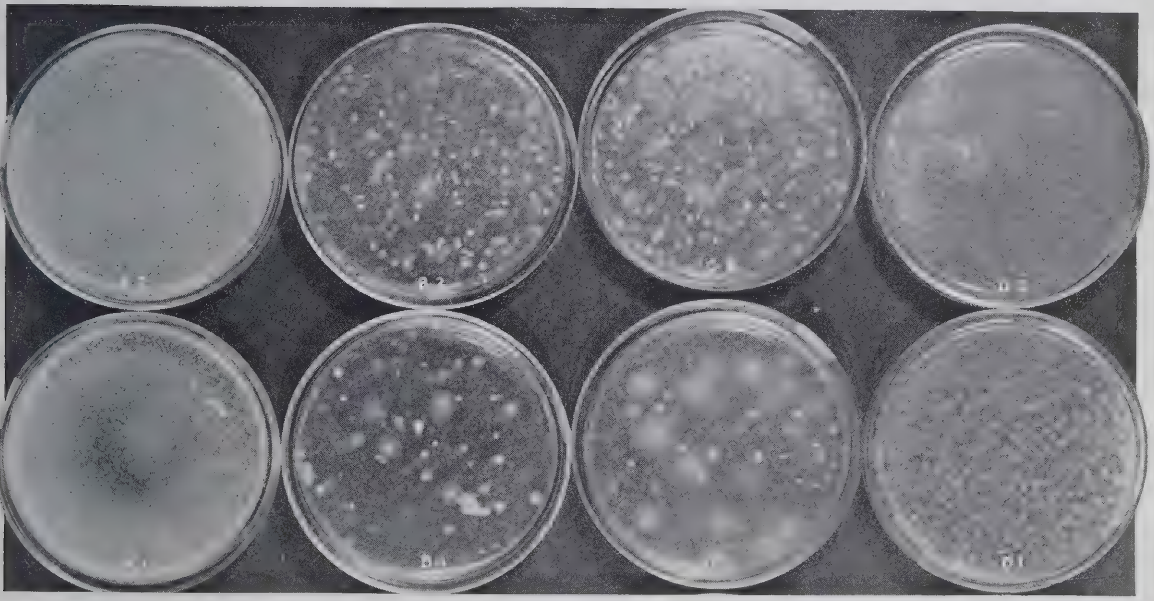


FIGURE 243. COMPARISON OF BACTERICIDAL PROPERTY OF BLOOD OF A NORMAL AND AN INFECTED RABBIT.

Another illustration of the difference in the bactericidal property of the blood of a patient with recurring attacks of rheumatic disturbances is shown in Figure 244, which gives two different dilutions of organisms in A, one marked 8x and the other 65x, where x is supposed to be a number approximately a thousand. When this quantity, approximately eight thousand, was placed in one cubic centimeter of my blood for ten minutes, the reduction in growth was reduced from that shown in A to that shown in B, the reduction being very great in both the eight thousand and the

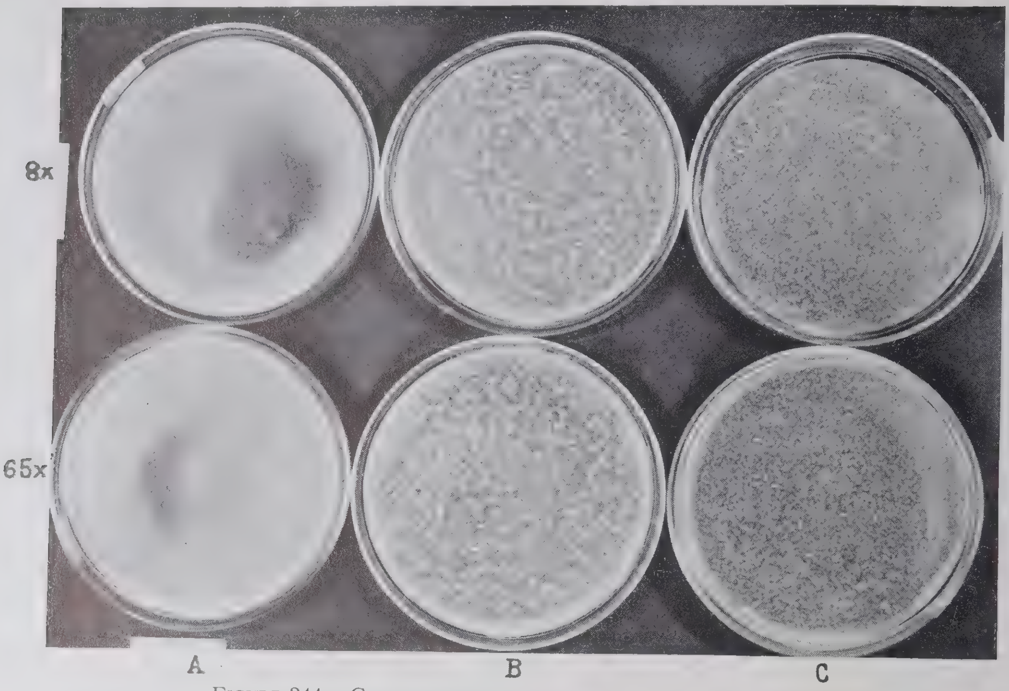


FIGURE 244. COMPARISONS OF BLOODS OF TWO INDIVIDUALS.

sixty-five thousand quantities of organisms. When these same quantities of the living organisms were placed in one cubic centimeter of the blood of this rheumatic patient for ten minutes, there was a reduction in the total number of organisms, as shown in C, but the reduction was not nearly so great as it was in the case of my blood.

At this point it would be well, perhaps, for me to make an explanation of the appearance of the Petri dishes. Bacterial cells, like plants, cannot grow normally if in too crowded a location. Consequently, in heavily inoculated Petri dishes the cultures are very small, each colony reserving about it an elbow room, so to speak; or rather, each takes from the soil nutrient material and gives off toxic material. Therefore the colonies tend to keep their individuality as units rather than coalescing; and the fewer organisms there are to grow in the space, the larger the colonies grow, just as a single tree will grow large with wide spreading branches, while crowded trees do not do this.

In Figure 241, I showed the difference in the bactericidal power of the blood of a rheumatic patient as compared with my own as normal, and called attention to the fact, that there was a zone of inhibition for a considerable distance around the blood on the

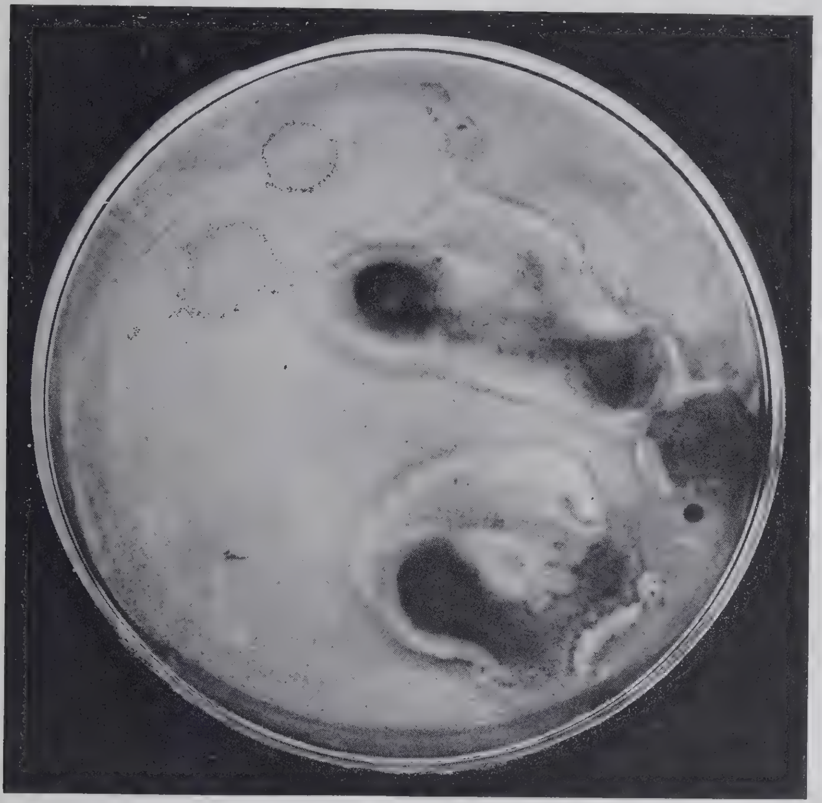


FIGURE 245. A BLOOD WITH A HIGH DEFENSE FROM A PATIENT RECOVERED FROM SYSTEMIC INVOLVEMENT.

infected agar plate. When such a patient has had infected teeth removed, which were apparently very materially disturbing the defensive factors, there is a marked improvement in this defensive quality of the blood, as shown by these various tests. Figure 245 shows such a case. This patient has returned to a vigorous normal health after having been ill for three years with symptoms variously interpreted as heart, digestive, and nervous system involvements. It will be seen here that his blood has now (three months after the removal of his infected teeth, during which time he has made a very rapid return to normal) become very highly defensive.

That infected teeth produce important changes in the blood can be shown in many ways. I have, in the preceding chapters, demonstrated their influence on the ionic calcium of the blood, the development of leucopenia, erythropenia, leucocytosis, etc.; and in Chapter 19, I illustrated the direct effect of the infection, whether injected or whether a tooth was planted beneath the skin of a rabbit, in reducing the hemoglobin. In this connection let me refer particularly to the experiments in Chapter 20 on Chemical Changes in the Blood, in which I showed that the placing of an infected tooth in either the blood of a patient or in normal blood tended to produce changes directly in the blood chemistry.

In order to determine, if possible, whether the tooth toxins tend to produce an hemolysis, I have placed extracts of infected teeth with blood and have also made comparisons of the effect of placing droplets of the blood, so exposed, on infected Petri dishes for comparison with normal blood or the same blood before exposed to the infected tooth. This is very excellently demonstrated in the colored plate in Figure 246, which shows in A three drops of normal blood placed on an infected agar plate; B, a similarly infected plate on which have been placed four drops of a patient's blood who was suffering from nervous breakdown and neuritis. It will immediately be seen that the organisms have grown well on and over the blood of the suffering patient, whereas the normal individual has greatly inhibited the growth on the infected plates. In C we have two drops of the patient's blood placed on a similar plate, but before doing so the blood was exposed to broken chips of this patient's own infected tooth, with the remarkable result that all the erythrocytes, practically, have been hemolyzed and the coloring matter has disappeared almost entirely from the droplets and is in solution in the free moisture in the margins of the dish. All of this suggests, if it does not demonstrate, that these teeth contain substances which have a very marked influence on the blood of the patient.

Another important study has been to determine the nature of the response that is called forth in the blood by the tooth toxin as compared with the bacteria from the tooth. To determine this we have vaccinated the drawn blood from rabbits and patients with dead organisms, to determine to what extent the blood was able to respond to increased attacking power; for, as Wright has shown, the defensive elements of the blood cannot be estimated, or, at least, are not indicated by the primary response to a bacterial invasion that is not great enough to call forth the greatest activity. I have, accordingly, taken the blood and subjected it to dead organisms of the kind that the media would later be inoculated with, and, after holding this vaccinated blood, containing a given amount of dead organisms, for from

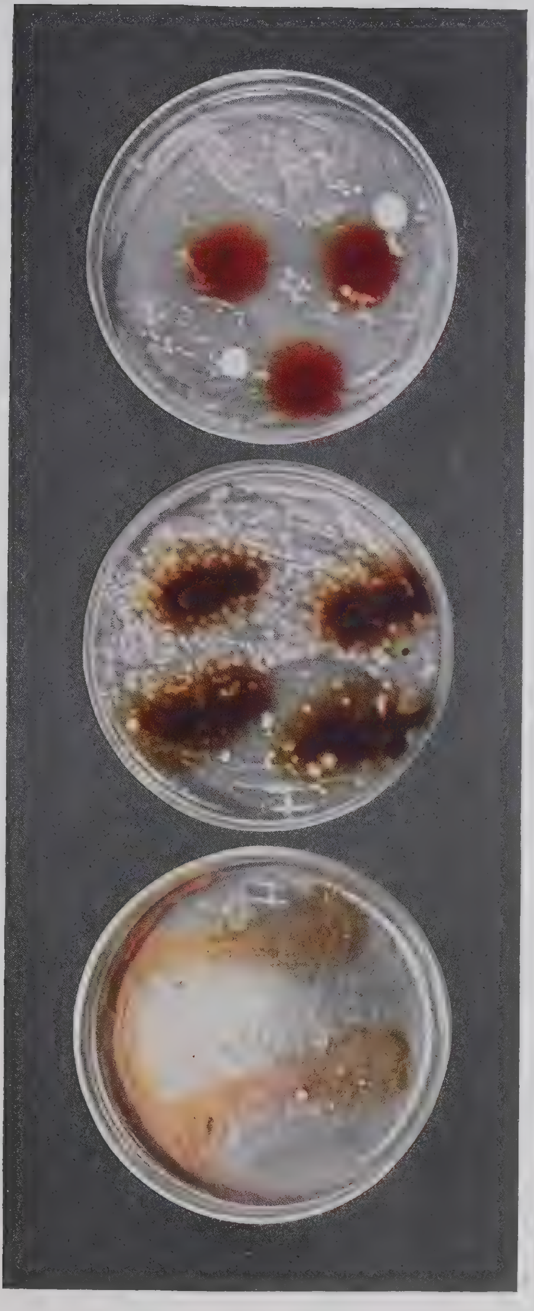


FIGURE 246. BACTERICIDAL PROPERTIES OF BLOODS: A, NORMAL HUMAN; B, BROKEN DEFENSE; C, BROKEN DEFENSE PLUS TOOTH TOXIN.

[CHAP. XLI—VARIATIONS IN THE DEFENSIVE FACTORS OF THE BLOOD.]

ten to thirty minutes, the living organisms were then placed in it for given periods of time; and it is quite remarkable that many individuals show a greatly increased activity of their blood from the presence in the blood of a small quantity of the tooth toxin prior to, if only for a few minutes, the placing in the blood of the living organisms for ten minutes. The bloods of some other individuals, however, make a very little response from the tooth toxin as an increased activity or efficiency. There is also a quantity factor. If the blood receives so small a quantity of the toxin as would be transferred to it by placing the tips of the roots of a freshly extracted tooth into the blood for ten minutes, a blood with a good reacting power will show a distinct improvement over the blood without that exposure to the tooth toxin. If, however, the blood is subjected to a considerable quantity of this toxic substance, such as putting the crushed pieces of tooth into the blood for an hour, it frequently practically paralyzes this reacting power, and the growth is many times more profuse than if a smaller quantity is used.

When the sterile, defibrinated, freshly drawn blood has placed in it some of the dead organisms, as stated above, their presence in the blood furnishes a chemical which acts directly upon the leucocytes, which quickly give off, as a result of this chemotactic reaction a bactericidal substance of very great power but which is not yielded to the blood until the stimulus is offered from the living or dead organisms, and either will accomplish the purpose. There is, therefore, an amount of dead organisms which will be most efficient for a given blood to induce it to its maximum bactericidal reaction.

In Chapters 3, 4, and 5, the results of the researches have indicated that there is a very distinct difference in the local structural changes in the mouth about dental infections, in patients having a low defense, from the reaction which occurs in the mouths of patients with a high defense. I have desired, therefore, to check carefully these different groups to see whether there is a distinct difference in the bactericidal properties of their bloods. It is necessary to keep in mind that, while all individuals may tend to have a mien, they may depart quite considerably from that mien. I have, accordingly, selected two patients on the same day, one presenting for prophylactic care. During his life he has had exceedingly little caries. The roentgenograms of his

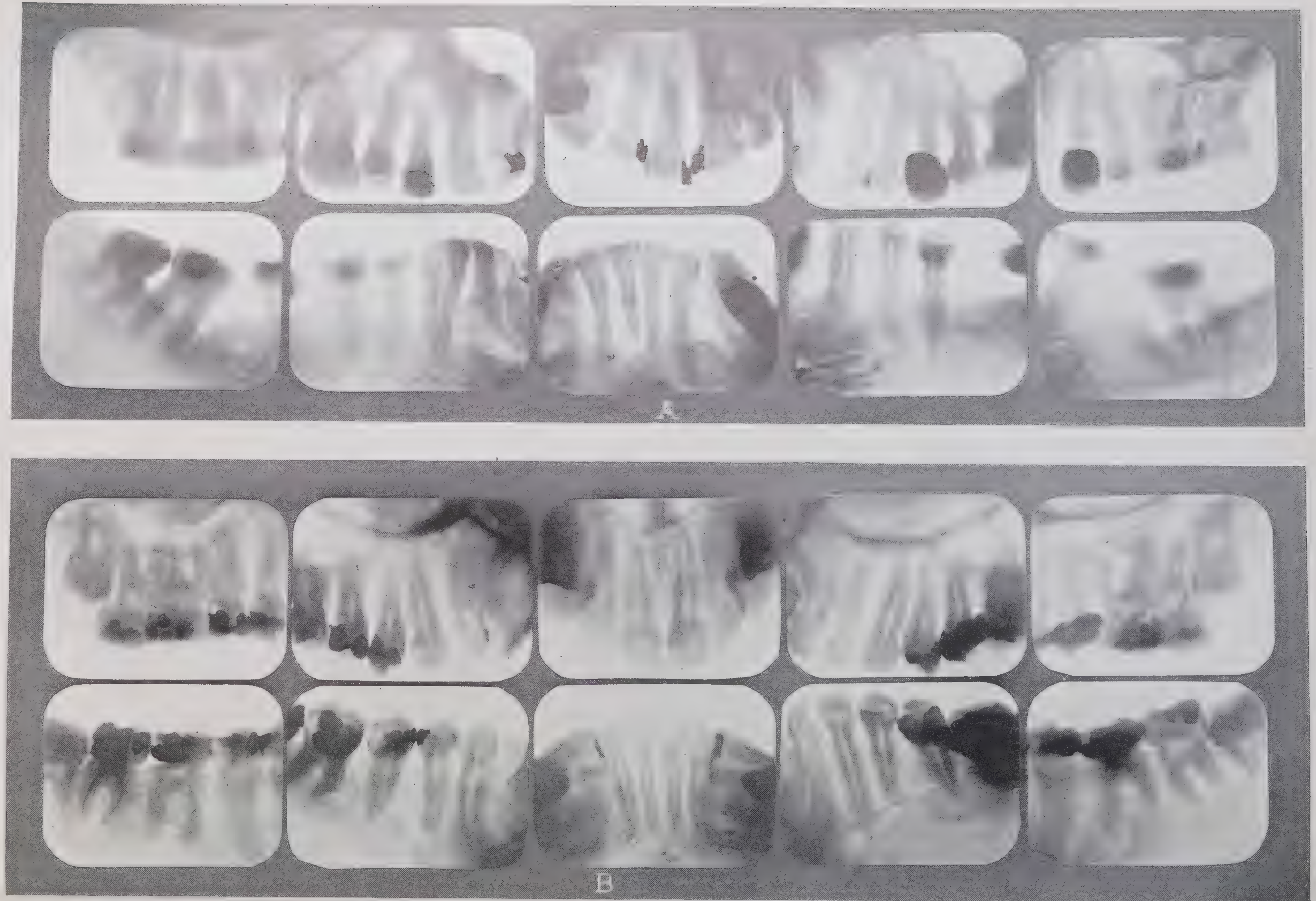


FIGURE 247. ROENTGENOGRAPHIC APPEARANCE OF THE TEETH OF THE PATIENTS REFERRED TO IN FIGURE 248. B, CASE NO. 1414, WITH LOW DEFENSE; A, 1415, WITH HIGH DEFENSE.

case are shown in A, Figure 247; and it will be noted that he has very extensive periodontoclasia. His age is about forty-five. He has never had any of the rheumatic group disturbances, nor have the members of his family. He is, accordingly, a typical illustration from the family history, his own history, and the local dental pathology, of the group with a high defense or absent susceptibility. His case number is entered as 1415.

The other patient (No. 1414) presents with symptoms of mild heart involvement, nervous exhaustion, and some neuritis. The roentgenograms of her teeth are shown in B of Figure 247. It will be noted that she has little tendency to gingival recession. However, she is young, her age being seventeen. She has several pulpless teeth, and notwithstanding a considerable quantity of pulp chamber unfilled, there is not extensive absorption of alveolar bone. In Chapter 43 I have shown the picture of the heart of a rabbit, inoculated with a culture from one of her teeth, having both endocarditis and myocarditis. This patient's father has had serious similar involvements, and his case is reported in Chapter 22.

I have, accordingly, undertaken to compare the defensive efficiencies of both of these bloods for combating streptococcal infection taken from dental source. The result is most striking and really remarkable, as shown in Figure 248, which shows two rows of Petri dishes, four for each of these two patients. The top two, marked A, are Petri dishes containing an agar culture medium suitable for growing streptococcus, planted with approximately one thousand streptococci. These are the controls. The other Petri dishes had the same quantity of the same kind of culture medium—namely, 15 cc.— and the same quantity of live organisms in each case except as follows: In B, before placing the thousand organisms in the Petri dishes they were subjected for ten minutes to contact with one-fourth of a cubic centimeter of the blood of one of each of these two patients. The germs and blood were then put into the Petri dishes which contained fifteen cubic centimeters, and as the germs were carried in approximately one-thousandth of a cubic centimeter of fluid, the additional fluid added to the Petri dishes in B was insignificantly more than in A, and the additional nutrient material only that quantity in a quarter of a cubic centimeter of blood.

It will readily be seen that Patient 1414, classified as an inherited susceptibility, did not furnish a blood capable of destroy-

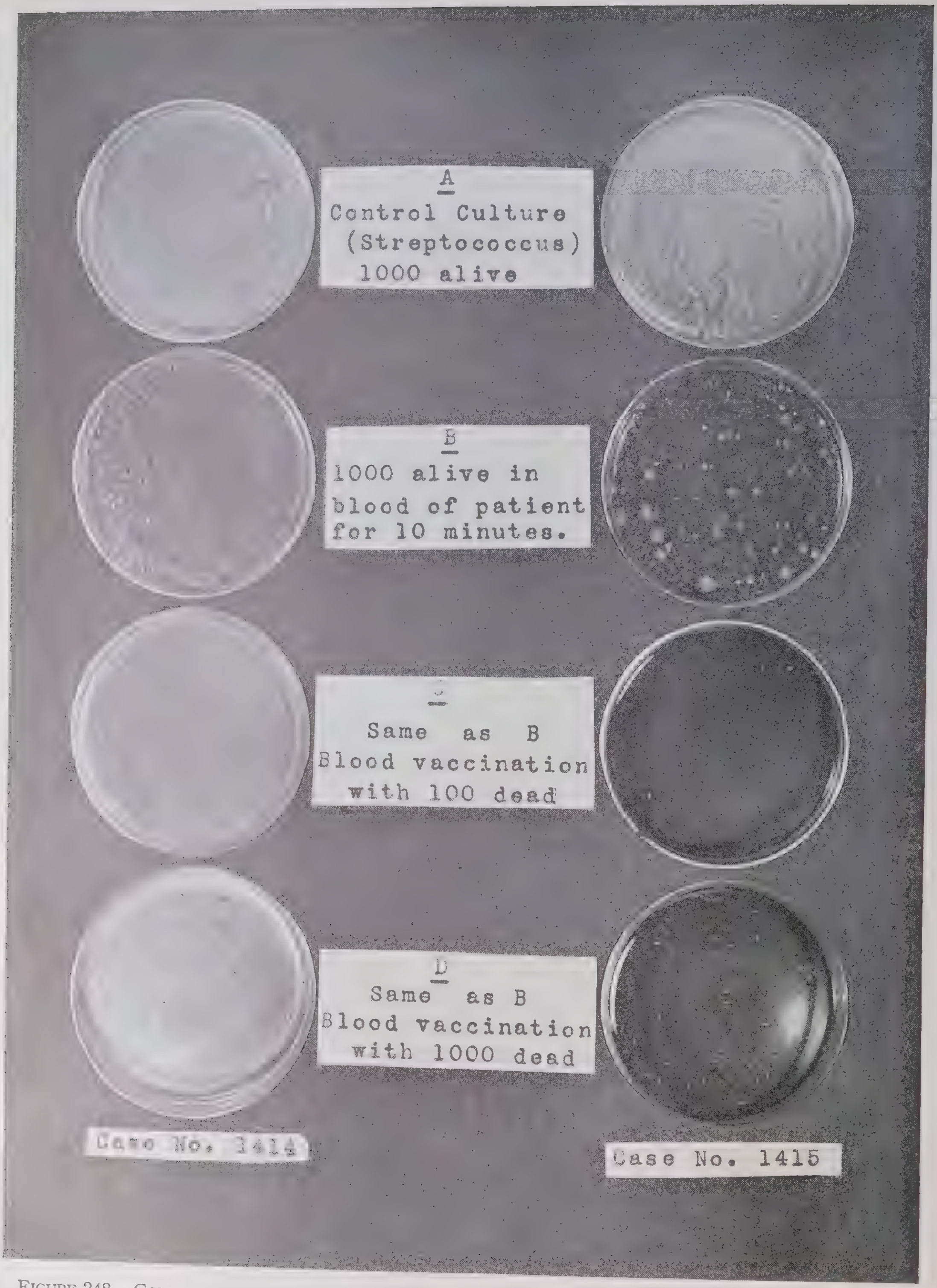


FIGURE 248. COMPARISON OF BACTERICIDAL CAPACITY OF BLOODS OF TWO PATIENTS PRESENTING SAME HOUR. CASE NO. 1414 HAS LOW DEFENSE WITH HEART INVOLVEMENT; CASE NO. 1415, WITH HIGH DEFENSE AND NORMAL. (SEE DENTAL CONDITIONS IN FIGURE 247.)

ing a very large number or proportion of the approximately one thousand organisms; but in strong contrast with this, the patient with the absent susceptibility, Case No. 1415, was able to destroy a large portion of the one thousand organisms with even that small quantity of blood in the remarkably short time of ten minutes. This we might take to represent the readily available resources of the blood for meeting an invading infection. But, as has been shown, the blood has normally a very high reserve defensive mechanism stored up in the leucocytes, which is capable, when called forth, to take care of very much larger numbers of organisms. I have, accordingly, then, endeavored to determine the relative capacity of these two individuals as representatives of their groups, for meeting an overwhelming or large infection, by placing in the same quantity of their bloods *in vitro* a given number of dead specimens of the same organism which we are using for testing. In C we have the effect on this quantity of organisms—namely, one thousand alive—by being placed in the blood of one of these two individuals for ten minutes as before, where the blood had been vaccinated for twenty minutes preceding with one hundred dead streptococci of that strain. It will be noted that the blood of Patient 1414 did not have the capacity for any greater response since more of the organisms of a thousand grew out than when the blood was not vaccinated, whereas the patient with the high defense, according to our classification by other means and by clinical histories, is shown to be correctly named, for the addition of these few dead organisms has called forth from his blood a chemical reaction which has devitalized practically every one of the thousand organisms in the small space of time of ten minutes.

We might assume, then, that Patient 1414, with low defense, did not respond because the vaccinating dose was not large enough. We, accordingly, made simultaneously with the preceding test, a determination of the effect of vaccinating for the same period—namely, twenty minutes—with one thousand dead organisms per one-fourth cc. of blood, in order that for every organism that was to be devitalized, one dead organism would be placed in the blood as an antigen to call forth that quantity of antibody. The blood of the patient with a low defense was not capable of responding to a greater degree with this relatively large vaccination, for,.in fact, her blood destroyed many fewer organisms than without the vaccination, and there seemed distinct evidence that the additional toxic effect of the thousand dead organisms embarrassed her blood to a marked degree, for when we compare the growth in D with that in A, we find her blood had almost lost its capacity for destroying bacteria, at least in that unit period of time. The patient presented in the other column, No. 1415, has been able to destroy almost all of the thousand organisms, but a few are growing, indicating that the toxic additive quality was sufficiently great to reduce the efficiency appreciably, since there was not approximately 100 per cent devitalization of the bacteria, as shown in C. We have, therefore, a type of evidence which substantiates the deductions in the preceding chapters, and I see no other explanation for the conclusion that the group of individuals represented as having the capacity for doing what Patient 1415 has done as compared with what 1414 has done, than that we are dealing with potentially two entirely different capacities for defensive reaction.

This illustrates too why the indiscriminate use of vaccines may have a very harmful effect in some instances while being distinctly helpful in others. Let us suppose that Patient 1414 had had a vaccine used in which the dilution and dosage was either of those represented, and probably any dilution between them. It would be almost certain that the vaccine would do more harm than good and that the patient would be made distinctly more ill. On the other hand, we readily see that if the patient in the second group received a vaccinating dose of either of these quantities, or probably any quantity between, his defensive mechanisms would be distinctly sharpened. As suggested, therefore, this becomes a means for determining *in vitro* those individuals for whom a vaccine may be expected to be beneficial and those for whom it will be injurious; and still more, by an extended series of these determinations, the particular dosage that will be most efficient for that individual can readily be estimated. This, therefore, should remove in the future much of the indifferent and negative result from vaccine therapy, and, as previously stated, we are indebted to Sir Almroth Wright for the development of this and much of the bacteriological and serological knowledge regarding the blood and its defensive mechanisms. The references to his work are very many and I have given the principal ones in the bibliography.

SEROPHYTIC MICROÖRGANISMS.

PROBLEM: What are the growth factors of microörganisms of the mouth in juices of living tissues?

EXPERIMENTAL AND DISCUSSION.

We naturally think of all of the forms of microörganic life as possible invading factors. It seemed wise to determine, if possible, to what extent the natural limitations of the various types of organisms would prevent their growth in normal tissue juices, assuming that dental infections are continually in contact with abraded tissue and that various forms of organisms have an opportunity to invade the vital structure. Since one of the first mechanisms of Nature's defense, when tissue is abraded, is to throw out the lymph, it is suggested as important to determine, if possible, which of the mouth organisms will grow in that fluid. I have, accordingly, placed sterile absorbent cotton beneath the skins of normal animals in order to collect a sufficient quantity of this material for experimental purposes. I have also obtained the same material by slow suction from the human. This material has been infected with mixed organisms of the mouth, including spirochetes, fusiform, long and short rod forms, micrococci, subtilis, diplococci, streptococci, and staphylococci. It is of great importance to note that almost invariably, so nearly so that it may be considered a constant rule, when animals are inoculated with mixed cultures, in many of the above varieties the only organism that is recovered from the lesions will be of the coccal group, and in more than 99 per cent of cases in our studies of the diplostreptococcal groups, there being less than 1 per cent staphylococcal infection also. It is not surprising, therefore, that when the human or animal lymph is inoculated with the mixed infection of the mouth, the streptococci and staphylococci grow out in the lymph of susceptible species or individuals, particularly the former, while the bacillary forms and spirochetes do not multiply, or at least do not in sufficient quantities to be found in the smears or tissue sections.

This research has been undertaken for two purposes: First, to determine what organisms tend to grow most readily in freshly extracted lymph and, second, as a means of comparing the lymphs of different animals. The table shown in Figure 249 shows a series of rabbits and rats in different conditions. Rabbit 1202 had sterile absorbent cotton placed beneath the skin for two hours, when it was removed and a couple of cubic centimeters of

LYMPH EXPERIMENT

	Lymph Dilution	Days Growth 1st Smear	Strepto-cocci		Bacilli		Days Growth 2nd Smear	Strepto-cocci		Bacilli		Days Growth 3rd Smear	Strepto-cocci		Bacilli	
			Gram-Positive	Gram-Negative	Gram-Positive	Gram-Negative		Gram-Positive	Gram-Negative	Gram-Positive	Gram-Negative		Gram-Positive	Gram-Negative	Gram-Positive	Gram-Negative
Rabbit No. 1202	Undiluted	1	—	—	—	—	2	+	—	—	++	10	++	—	—	±
	Dilution 1:5	1	+	—	+	—	2	—	+	—	—	10	++	—	—	±
	Dilution 1:1	1	++	—	—	+	2	++	—	—	—	10	+++	—	—	±
Rabbit No. 1222	Undiluted	1	—	—	—	—	2	++	—	—	—	10	+++	—	—	±
Rat-Normal Diet	Undiluted	1	—	—	—	+	4	+	—	—	+	6	+++	—	—	+
Rat-Deficiency Diet	Undiluted	1	+	—	—	++	4	+	—	—	++	6	+++	—	—	±
Rat-Deficiency Diet	Undiluted	2	—	—	—	++	3	±	—	—	++	4	+	—	—	+
Human Serum Case No. 335		2	++				10	++++								
Case No. 1421		2	++				10	++++								

FIGURE 249.

lymph expressed into sterile tubes. Dilutions of one to five, one to one, and full strength, were tested, as was lymph similarly drawn from Rabbit 1222, by inoculation with the mixed flora from highly infected gingival pockets. The chart shows three different succeeding dates and the type of streptococcus, whether positive or negative, and the type of bacillary form, whether Gram-positive or negative, which grew out. It will be noted that the undiluted lymph from the two rabbits gave no growth in twenty-four hours, whereas the dilution of one to five gave a slight growth of Gram-positive streptococci and of Gram-positive bacilli. The forty-eight hour culture, however, showed Gram-positive streptococci in both the undiluted and a Gram-negative bacillus in the other. The ten day growth showed a more abundant Gram-positive streptococcus and diplococcus, and Gram-negative bacilli. The organism, however, which grew out in the majority of instances and most profusely, was the Gram-positive streptococcus. The three rats—shown in the same chart, CHANGES IN RATS WITH PLANTED TEETH—NORMAL AND DEFICIENCY TEST

	Diet		Original Weight at Inoculated Date	Weight Changes						Days Tooth Retained	
	Normal	Deficiency		3 to 4 Days	6 to 7 Days	8 to 9 Days	10 to 11 Days	15 to 16 Days	20 to 25 Days	Normal	Deficiency
Group I Normal Diet	+		122	120	110	119	122	139	173	6	
	+		192	179	185	187	186	194		9	
	+		124	126	127	129		133		13	
									Average	9	
Group II Deficiency		+	79	86	90	91	95	93	106		40+
		+	84	87	91	92	88	96	101		40+
									Average		40+
Group III Pregnancy			139	136	135	140	134	142	134		6
			184	186	123	122	125	129	149	9	
			285	291	239	244	222	230		14	
									Average		9

FIGURE 250.

had lymph removed in the same manner, and it will be noted that in general the same condition obtained though the growth was exceedingly weak at first. We find ourselves unable to determine when an infected lymph has degenerated to a point where it ceases to be comparable to normal circulating lymph, and it is probable that after twenty-four hours it should be considered that its bactericidal properties would be greatly reduced. In the study of the rats, however, it will be noted that the second rat serum showed a Gram-positive streptococcus in twenty-four hours, but it may be significant that this rat was on a deficiency diet, as compared with the one preceding which was on normal diet. There is also a greater growth at the end of twenty-four hours in the Gram-negative bacillary forms in both the rats on deficiency diet.

These and other results suggested the desirability of repeating on the rats some of the experiments that had been made on rabbits by the implantation method. The table in Figure 250 shows a series of these results. Teeth were implanted beneath the skins of rats, and their weights were taken on succeeding days. The results are strikingly different from those which were obtained by placing similar infected teeth beneath the skins of rabbits. It may be argued that a human tooth is a relatively large quantity of infection to place beneath the skin of a rabbit, the quantity effect, therefore, accounting for the high mortality from that operation. If this quantity factor be true of the rabbits, it must of necessity be infinitely more true of the rat, which is approximately one-tenth the weight of a rabbit. It is most interesting to see, however, that in practically every instance these infected teeth have produced practically no serious effects on the rats when they were on normal diets, as estimated by their change in weight, for they have gone on gaining quite like the controls. The only difference discernible has been that they are not so active in their cages, tending to sit quietly in a corner, and this is particularly true of those on deficiency diets. When we compare, however, those rats that were on a deficiency diet, with those on a normal diet, there is a marked difference.

When an infected tooth is placed beneath the skin of a rabbit, the reaction almost immediately resolves itself into one of two processes: either there is formed a capsule, highly vascularized and which apparently acts as the defensive mechanism built about the structure, in which case the rabbit lives, or there is a more or less active local degeneration accompanied by very definite changes in the ionic calcium of the blood, the alkali reserve of the blood, the ratio of polymorphonuclears to lymphocytes, etc. In exceedingly few cases, however, does a rabbit ever expel by a local suppurative process the infected tooth so planted. On the contrary, however, rats with their higher defenses will build an encapsulation about the tooth, break down a gateway to the surface in an astonishingly short period, as shown in the chart in Figure 250, in which it will be seen those rats on a normal diet shown in Group 1, have expelled the tooth in from six to thirteen days, with an average of about nine days. The rats on a deficiency diet, however, (see Group II) required over forty days on an average to expel an infected tooth. In Group III, we have undertaken to get data that would enable us to make comparisons between rabbits and rats with regard to their defense at the time of pregnancy and the effect of such a foreign implantation in that condition. The data available are not sufficient for extended conclusions. In general, however, pregnant rats did expel infected teeth about as rapidly as did the rats that were not pregnant. In the chapter on overloads I have shown that when rabbits are injected with dental cultures during pregnancy, there is a tendency to abortion or to the death of the fetal forms, with or without the expulsion, and with great danger to the life of the mother rabbit. Since the period of gestation with rats is so short—namely, three weeks—it is exceedingly difficult to determine whether the effect of tooth implantations tended to hasten confinement. The effects are distinctly different, however, on rats than on rabbits, since the offspring of pregnant females carrying implanted teeth seem to be normal and develop as though no such overload had been placed upon them, whereas with rabbits, results were nearly always fatal to the offspring. They were either stillborn or lived but a few hours. A typical illustration of this effect is shown in Figure 251, in which will be seen two rats in the backs of which infected teeth were planted. One has completely expelled the tooth in nine days, and the other in thirteen. In the latter, however, the tooth is just in the process of exfoliation.

SUMMARY AND CONCLUSIONS.

1. While this study is, as yet, very incomplete, sufficient progress has been made to indicate that there is a very great difference in the defensive mechanisms of different species of animals. From these studies and from determinations made by the method presented, it is apparent that the rabbit and rat have distinctly different capacities for defensive reactions to dental infections.

2. The bactericidal property of the blood and lymph of rabbits was very similar to that of the human, though under normal conditions apparently not subject to so great variations.

3. The organism which tends most readily to grow out in the lymph and blood serum of humans and of animals, is a Gram-positive streptococcus, which corresponds to our studies reported in other chapters regarding the organism isolated from involved tissues of animals which have been inoculated with mixed cultures from human dental sources.

We see from the above that there is a great variation in the bactericidal properties of different bloods, whether of animals or humans, and that this quality of high or low defense relates directly to our groupings of individuals with or without systemic involvements from dental and other focal infections, and that the bactericidal quality can express itself in even one minute's time to such a marked extent as to destroy a large proportion of the organisms exposed to the blood. We would, therefore, briefly express this quality in the following conclusion:

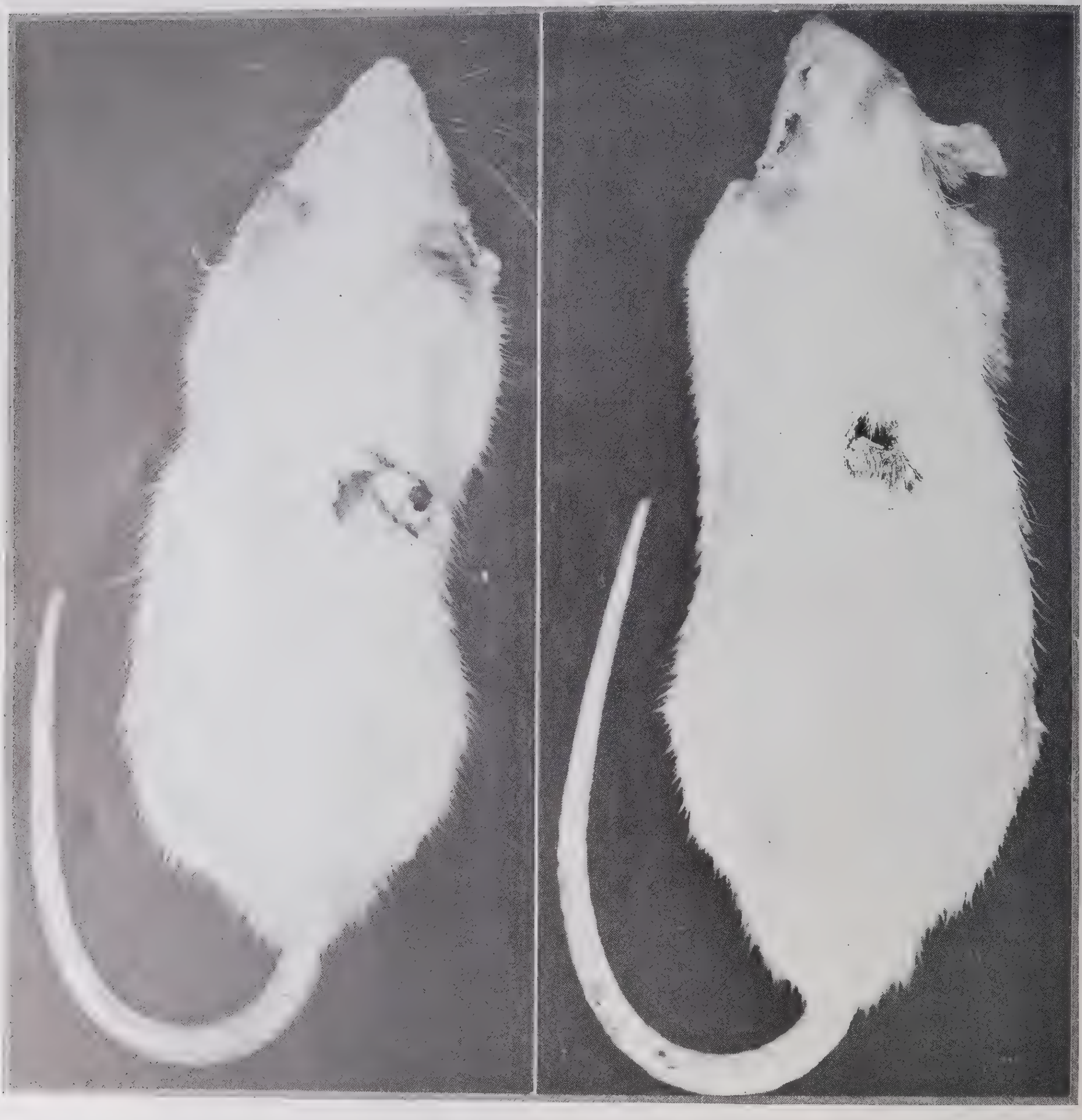


FIGURE 251. Two rats with teeth planted beneath the skin, one completely extruded and the other nearly so. Their high defense makes this possible.

There is a marked difference, which is very readily measurable in the bactericidal properties of the bloods of individuals of high defense, as compared with those of low defense to systemic involvements from dental infections.

When the mixed flora of the oral cavity is planted in the normal blood serum or lymph, the varieties that grow are almost entirely limited to the strains of diplo- and strepto-cocci, with occasional staphylococci, with the diplo- and strepto-cocci largely predominating.

CHAPTER XLII.

METHODS FOR REINFORCING A DEFICIENT DEFENSE.

PROBLEM: Can a temporarily or permanently low defense against the streptococci of dental infections be increased or enhanced either temporarily or permanently?

EXPERIMENTAL AND DISCUSSION.

In the preceding chapter we have seen first that there is a great variation in the defensive factor of different individuals as expressed in the bactericidal property for streptococci of dental origin, and also that this quality regularly diminishes in rabbits when they have been subjected to implantation of infected teeth. The researches there reported also indicate that the defense of an individual tends to go up with the removal of chronic dental infections. But many of our patients do not come back readily to normal. If a sapling be broken over, it may straighten nearly to its original position. If, however, it can be supported, as being tied to a stake, it much more rapidly will repair the injured timber and probably recover its original strength. Just in proportion, however, as that sapling may have been held crushed over to the ground for a long period of time, or its defensive factors injured by any other means, the prospects for a complete recovery are rapidly diminished; and if it should be that the timber in question is that of an old tree, the repair may be much less vigorous, and the obstacles that will be safely overcome much less, than with the young tissue.

Similarly, many of our patients come to us with overloads that have been present for so long a time that, even though they are removed, the defense is very greatly lowered. In many instances the overload is one that cannot be reached or removed, and it therefore cannot be subtracted. In still others the overload consists of an inherited deficiency in the mechanisms of defense, for we have seen in the preceding chapter that the individuals constituting our first group in susceptibility—namely, those with absent susceptibility—have by inheritance a high defense, and they show an unusually high bactericidal property of the blood.

In the second group—those with an acquired susceptibility—while in that state we find that they have a lowered defense below their normal at other times, but that they tend to come back to their normal with removal of overloads. In other words, the bactericidal property of their blood is temporarily depressed by their overloads, one of which overloads is very often a dental infection. The third group—those with an inherited susceptibility—always have an abnormally low defense against streptococcal infections; and their normal, which is poor at best, tends readily to be still more depressed with overloads. They are in a state in which the normal unstimulated defense of the blood is not adequate to protect them against streptococcal and staphylococcal invasions. In the recurring active combats with this type of infection, as any of the rheumatic group lesions, they whip themselves up to a defensive reaction adequate to make them temporarily relieved. They are, however, dependent upon this secondary defensive mechanism which must be called into play frequently and vigorously, and, accordingly, they have what they call attacks of their disturbance which are largely records of remissions and exacerbations.

When, in any individual the normal defensive mechanism is not adequate and the infection continues to develop and increase in quantity, the very increase, which endangers the host, is the mechanism which sets in motion the defensive machinery constituting the secondary defensive systems of the patients. These secondary defenses are largely in the blood and tissue cells of the body, probably mostly in the leucocytes of the blood. For years as we have studied these patients with their chronically low defenses, we have realized that the desideratum in their behalf was to find some reinforcement which could be brought to their aid to supplement their defensive systems. We readily visualize how the antitoxin for the diphtheria toxin is developed by the horse and can be readily transferred from the horse's blood serum to that of the patient, with the result that a sufficient reinforcement is added to turn completely the tide of the events; and the individual whose death was certain or life despaired of, because of his losing the fight with that organism, finds the table turned, and thanks to the defensive substances contributed by the horse, the patient is now able to make a winning fight and the organisms are annihilated from his system or rendered so innoxious to him that the body ignores them, in which case he may become a carrier.

But the toxin developed by the diphtheria bacillus is an exotoxin, and the streptococci and diplococci with which we are concerned develop largely endotoxins, and it is a very different matter to produce outside the body of the host a substance which will be bactericidal or antitoxic of such a degree as to make a comparable reinforcement to that made by the diphtheria antitoxin. Indeed, we seem to be dependent upon bactericidal substances that are generated within the blood and tissues of the host for defense against this organism. We, therefore, come back continually to the program of using vaccines, preferably made from the particular strain of organism that is producing the disturbance. I have been using these autogenous vaccines for over ten years with very variable results. In many instances the vaccines seem to have little, if any, beneficial effect; and, indeed, in a few cases they seem to be positively to the patient's disadvantage, while in other cases they seem to work like magic. With their use many patients have been seen to make a most definite increase in the rapidity of their mastery over the invading infection. Several of these are discussed in the chapters on systemic involvements; and in several instances where patients had been either completely or nearly bedridden for years, they have been put back on their feet by changes that have been produced, apparently, by the removal of dental focal infections and the stimulating of their lowered defenses by use of a vaccine.

To be more specific, the patient shown in Chapter 64 had been bedridden for five years with deforming arthritis. The removal of her dental infections produced but little change. The use of the vaccine made from those dental infections made so great improvement that she was on her feet in five months' time, and for two and one-half years she has had no recurrence sufficient to put her back in bed. She now does all her housework except the laundry. This result was produced with an autogenous vaccine.

Similarly, the case shown in Chapter 64, who had been bedridden for four years, completely helpless, has now for several years been doing her housework, and continues practically free from rheumatic disturbance and progressively improved, apparently largely the result of the vaccine together with the removal of the dental infections.

Similarly, we might review many cases. Note that while many cases have responded beneficially to the use of a vaccine, many others have shown no improvement, and this we were able to determine only after trying and failing. All of this has suggested that ultimately we must find some substance which may be added to the patient's defensive mechanism and thereby help him or her directly to combat the infection. Again we are greatly indebted to Sir Almroth Wright for splendid suggestions, for he has shown that this process of vaccination of the blood is quite as effective *in vitro* as *in vivo*; and we have, accordingly, taken that suggestion and tested the bloods of the patients presenting for diagnosis and means of assistance in the defense against their infections.

In general, we find that while there is a great difference in the response of the blood of different individuals, they tend, in general, to show a capacity for a greatly enhanced bactericidal efficiency of their blood by the introduction first into their blood of dead organisms, we now think preferably of the strain for which the bactericidal quality is being determined. The difference in different patients is so great, that whereas a very few dead organisms will suffice to call forth from the blood this secondary defensive factor in some cases, in other cases a larger quantity of dead organisms are required to do so. There is also a very great difference in the extent of this reinforcement for secondary defense, as determined by the number of organisms that will be killed by a given blood after being vaccinated *in vitro* with varying amounts of dead organisms of the same strain. The blood of some patients reaches its maximum efficiency with the addition of a very few dead organisms per unit volume, where others do not have the maximum efficiency called forth until a large number of dead organisms are added; and, similarly, whereas some bloods will kill off a large per cent, or nearly all of the living organisms, they are aided after being vaccinated, whether that quantity of live organisms be five per cubic centimeter or five thousand, or even fifty thousand, some other bloods will reach their maximum capacity with a few hundred bacteria. In other words, there is a very great difference in the capacity of different bloods for reaction, as well as a very great difference in the quantity of dead organisms that are required to produce the most efficient reaction.

MEANS FOR COMPARING AND CLASSIFYING THE DEFENSIVE FACTORS OF PATIENT'S BLOOD.

Since, as we have shown, there is a very great variation in the bactericidal property of these various patients, when considered individually, and in the groups when considered as such, it becomes very desirable to evaluate this defense in comparative terms. This has suggested the development of the system of uniform observations and determinations to be made on various individuals being studied, in order that we may establish, ultimately, a group of standards which will express the limits that may be placed on both an adequate and inadequate defensive mechanism. After working out several combinations of tests and controls, the one that we are using at the time of this writing as being the most simplified to date, is shown in Figure 252. These forms are used as the outline for the different determinations and the results are checked directly into them, and they lend themselves to modifications when such are desired. The Petri dishes are numbered in accordance with the numbers in the column to the left, and we soon come to know what tests any given number represents.

All of the study of this phase of our problem—namely, the mechanisms of defense of the blood and the means for their strengthening—have suggested the necessity for the development of other means than the use of vaccines for the strengthening of the defense. To do so has required further knowledge of the nature and structure of the substances chiefly instrumental in elaborating or generating these defensive factors. Wright has shown, as we have repeatedly verified, that the simple process of heating the vaccinated blood before its vaccination with the dead organisms entirely inhibits the enhancement of the bactericidal property, and this because the leucocytes are devitalized at 48° C. It is therefore possible to determine very exactly and directly the amount of the defensive substances already in the blood before a reinforcement is drawn from the leucocytes. We have, accordingly, demonstrated that in some individuals with a chronically low defense the amount of defensive element present in the blood, without calling forth any material from the leucocytes, is exceedingly low, and in some others we find that the leucocytes tend to contribute this reinforcing immunity with a small amount of stimulation from the presence of dead organisms or from toxin, while others require a much larger quantity of stimulation. Another and most striking feature which we referred to in the preceding chapter is the fact, that most bloods of a high defense will develop this secondary defense within one minute after the placing of the tooth toxin or

BACTERICIDAL POWER OF BLOOD

Patient Case No. Date

Serial No. of Plate	Patient	Blood			Media		Vaccinated Dead Organisms and Time Exposed			Live Organisms and Time Exposed			Tooth Toxin			Results
		Normal Control	Quan Used		agar	other	100 50	1,000 500	10,000 5,000	100 50	1,000 500	10,000 5,000	Patients	Misc.		
			drops	cc.												
1	✓		2		✓											
2		✓	2		✓											
3					✓					Ctl						
4					✓						Ctl					
5					✓							Ctl				
6					✓		Ctl									
7					✓			Ctl								
8					✓				Ctl							
9	✓			1	✓					10						
10	✓			1	✓						10					
11	✓			1	✓							10				
12		✓		1	✓					10						
13		✓		1	✓						10					
14		✓		1	✓							10				
15	✓			1	✓		20			10						
16	✓			1	✓			20		10						
17	✓			1	✓				20	10						
18	✓			1	✓		20				10					
19	✓			1	✓			20			10					
20	✓			1	✓				20		10					
21	✓			1	✓		20					10				
22	✓			1	✓			20				10				
23	✓			1	✓				20			10				
24		✓		1	✓		20			10						
25		✓		1	✓			20		10						
26		✓		1	✓				20	10						
27		✓		1	✓		20				10					
28		✓		1	✓			20			10					
29		✓		1	✓				20		10					
30		✓		1	✓		20					10				
31		✓		1	✓			20				10				
32		✓		1	✓				20			10				
33	✓		2		✓								30			
34	✓			1	✓					10			30			
35	✓			1	✓						10		30			
36	✓			1	✓							10	30			
37		✓		1	✓					10			30			
38		✓		1	✓						10		30			
39		✓		1	✓							10	30			
40																

FIGURE 252.

dead bacteria from same, whereas the blood of other individuals will require several minutes (ten to fifteen) to develop the defensive factors. We have also found that this quality varies through considerable range whether a rabbit is normal or has been under the strain of a dental infection such as the planting of an infected tooth for some days. This latter indicates to us that the presence of the dental infection has decreased the capacity of the leucocytes for reaction, as well as the important data brought out in Chapters 19 and 20 showing that the presence of the infection reduces the number of leucocytes or produces a leucopenia, chiefly a depression of the polymorphonuclears, and also depresses the ionic calcium of the blood. All of this has suggested that the whole problem resolves itself very largely, if not quite entirely, to one of chemotaxis.

In this connection we think immediately of the capacity of certain drugs to act specifically on certain infections. This is quite strikingly illustrated in the effect of quinine on the malaria plasmodium, and of the arsenic compounds, such as salvarsan, on the Treponema pallidum. We also think of the action of the salicylates which have been used so extensively in the treatment of rheumatic affections. I will, accordingly, report here under the studies of the mechanisms for the increase of defensive mechanisms of blood, some studies we have made with the salicylates.

Some years ago I inoculated two groups of rabbits with proportional amounts of a culture producing acute rheumatism, and treated the one group with the sodium salicylates and the other without. I was never sufficiently satisfied with the results to publish them, since I could not interpret them. The evidence indicated that the rabbits receiving the sodium salicylate of the doses I was using lived longer, but with reinoculations with the same strain, the evidence suggested that a larger percentage of the rabbits developed heart lesions. I was never able to determine whether the test had important significance since there were no data on what should constitute a proper and what an overdose of that drug for rabbits, and it would be very clear that any overload, such as an overdose, might be distinctly harmful.

More recently I have had an opportunity to make a different type of study directly on the human. A patient with acute deforming arthritis presented for our study, reporting that he had been getting progressively worse, that the only drug that seemed to give him any relief was some form of salicylate, and that he had come to the point that even this had to be taken in such large doses that its continuance seriously disturbed his digestion, and that his physician was now administering it intravenously three times a week. I suggested to him that before anything was done to disturb dental infections or any other of the factors involved, we make studies of the changes in the ionic calcium of the blood, if any, accompanying and following the intravenous injection of the sodium salicylate. Results were most striking. The ionic calcium of his blood at the time was running at approximately 7. With each intravenous injection the ionic calcium of his blood would drop to the neighborhood of 6, and in about twenty-four hours it would ascend to 9 or above, and in another twenty-four hours would return to about its original level.

Coincidentally, there was a parallel change in his symptoms. Within an hour after the intravenous injection of the sodium salicylate by his physician, sometimes within thirty minutes, (for he came directly, according to our mutual arrangement, from one office to the other, a distance of a few blocks,) he developed a profound depression amounting to a rather extreme negative phase. This usually lasted for about five hours, when it gradually disappeared and in its place came a sense of well being, great relief from his rheumatic symptoms, and with it a displacement of the mental cloud with one of hope and confidence and general well being. This latter usually lasted about twelve hours, after which he gradually subsided to his old level. The history of his case was very similar to that of general clinical practice: namely, that the symptoms as pain were greatly relieved by the use of the salicylates; that the system needed to be pretty well saturated to develop this reaction; that the results were relatively transient, requiring quite frequent and continuous repetition. We have, therefore, in this case an illustration of the direct effect of chemotaxis in influencing the defense and also indicate one, at least, of the changes occurring in this patient's blood. We were not at the time of this series of determinations making bactericidal determinations of the blood. This has since been done, for he is still suffering and almost an invalid with his deforming arthritis. The changes in the ionic calcium of this patient's blood, as shown by the various determinations

IONIC CALCIUM, SODIUM SALICYLATE, AND DIET FACTORS

Date	Sugar	Non protein Nitrogen	Uric Acid	Biological Determination				Chemical Determination	
				Calcium Ionic	Calcium Ionic and Combined	Calcium in Combination	Thrombin	Calcium	Alkalinity Index
8-17-22					10.625				
8-24-22				6.67	9.81	2.14			
8-24-22				7.85	8.34	0.49			
8-24-22				**10.00**	**11.11**	**1.11**			
8-26-22				**5.51**					
8-28-22				7.49					
8-28-22				6.67					
8-28-22				6.34	8.76	2.42			
9- 2-22				6.67	9.02	3.55			
9- 5-22	105	47.5		6.67	9.33	2.66		10.87	
9- 8-22				6.68	9.72	3.04			
9-11-22				7.27	8.73	1.46			
9-13-22				7.52	9.52	2.00			
9-19-22				7.00	9.23	2.23			
9-21-22				8.10	9.87	1.77			
10-18-22				7.54	12.08	4.54			23.3
11-23-22					12.82		12.68		
12- 8-22	103		3.25		12.10		13.46		
3- 7-23	93	26.5	2.85	12.206	14.34	2.85	6.79		
4-19-23	95			12.061	13.34	1.279	6.539		

FIGURE 253.

are presented in Figure 253. It is important to note that after this patient went on a forced milk diet, taking large quantities, his ionic calcium has increased from a level at about 8, frequently being as low as 6 and a fraction, to 12; and while, when last seen, he thought his general condition was somewhat improved, his actual improvement has been slight; and it is apparent that the depressed ionic calcium of his blood is not the principal factor in his lesion. The bactericidal property of his blood is exceedingly low, and the condition strongly suggests that if some bactericidal element could be used to reinforce his own normal defense, he would make much more rapid progress. He has had dental focal infections removed with but little improvement in his general condition. He has had vaccines used and these do not call forth the needed defensive response from his blood. He seems quite unable to manufacture the bactericidins required for defense against this infection. Since the removal of his dental infections, he has been under treatment for chronic colitis, which has existed for years and which is undoubtedly contributing to his general condition, and, indeed, it is not improbable that the infection there is furnishing a toxin which is destroying his defensive mechanism or neutralizing its efforts. I have reviewed this case in this detail to illustrate a condition which exists in a very large number of the patients with marked rheumatic susceptibility, and thus emphasize our limitations and thereby stress the need for more intensive effort.

Another means of approach to this problem has already been discussed in the chapter on the Glands of Internal Secretion, and it has been instructive to find that whereas a given tooth from one of our patients, at the time of this writing has killed thirty-three rabbits in an average of four days, the use of injections of extract of parathyroid not only seemed to increase the resistance of the rabbit, as judged by the length of its life which was ten days (only one other rabbit in the series having lived to that length and it an unusually large one) but perhaps more important, following the injections of the parathyroid, this rabbit's ionic calcium was increased, for, whereas in other rabbits the ionic calcium progressively decreased quite continuously and regularly, this rabbit's calcium, which was 7.2 before the injection, increased to 10 the following day, which change occurred on two different occasions. This has suggested quite strongly, since this parathyroid was injected subcutaneously around the implanted tooth, that there may have been a local reaction between the parathyroid substance and the toxic material of the tooth. Studies are now in progress to throw further light on this phase of the question.

It is of particular interest to note that we have frequently seen in individuals a very prompt increase in the ionic calcium of the blood from the administration of parathyroid and calcium lactate, one or both. Such cases are cited in the chapter on the Glands of Internal Secretions. In one case, for example, in two weeks' time the ionic calcium of a woman suffering from rheumatism increased from 8 to 10, and in the two weeks' time her depression and discouragement had completely given way to one of cheerful confidence and joy of living, together with relief of the rheumatic symptoms. It must be stressed that this work is still in the experimental stage and the members of the profession must not rush headlong into the administration of this and other drugs until further experimentation under controlled conditions shall have been made.

For considerable time I have been making studies with other drugs to ascertain, if possible, whether or not beneficial results might justify their use for reinforcing an abnormally low human defense. I have found two drugs in particular to be apparently helpful in increasing the defense of rabbits. One of these, ethylhydrocupreinhydrochlorate, enabled the rabbits that had been prepared by its use to withstand approximately eight times the lethal dose of infection when inoculated intravenously. Some of these rabbits, however, developed untoward symptoms, particularly in the rabbits' eyes. I have since learned of work that has been done with this drug by different observers in the treatment of pneumonia, some of which patients developed eye complications, and there has been a difference of opinion as to the extent to which this drug was involved in the secondary involvement. Another drug which has been studied is the active principle of chaulmugra and its compounds. These have been reported in Chapter 26 on Chemotaxis. It is sufficient to state at this point that these drugs, while showing promise and encouragement for the future, do not yet furnish us with the reinforcing chemicals or medications which will change an individual from one with an inherently low defense to one with an adequate defense. Our interpretation of the application of these principles will be given in succeeding chapters.

Our studies of the nature and extent of the reinforcement of the defensive blood *in vitro*, bring out many points of important information. Some individuals react in accordance with what might be anticipated, while others do not, for they may look comparatively well and strong and, upon examination, prove to have a low factor of safety. A striking illustration of low defense, which, however, I had anticipated, is that of a woman suffering from recurring attacks of rheumatism and iritis, with a general bacteremia, the organism having been recovered from her blood on many occasions. When this patient's blood was tested for its capacity to kill organisms, it was found to be very low; but the most striking feature was that the use of dead organisms placed in this patient's blood *in vitro* for even thirty minutes, almost completely failed to call forth the secondary response. Even the placing of large numbers of dead organisms failed to increase the efficiency of her blood.

Another striking illustration is the following, which is shown in Figure 254: Case No. 1417.—This patient was suffering from osteomyelitis. He had lost twenty-five pounds in two weeks' time. His freshly defibrinated blood had its maximum bactericidal capacity without the addition of dead bacteria. The

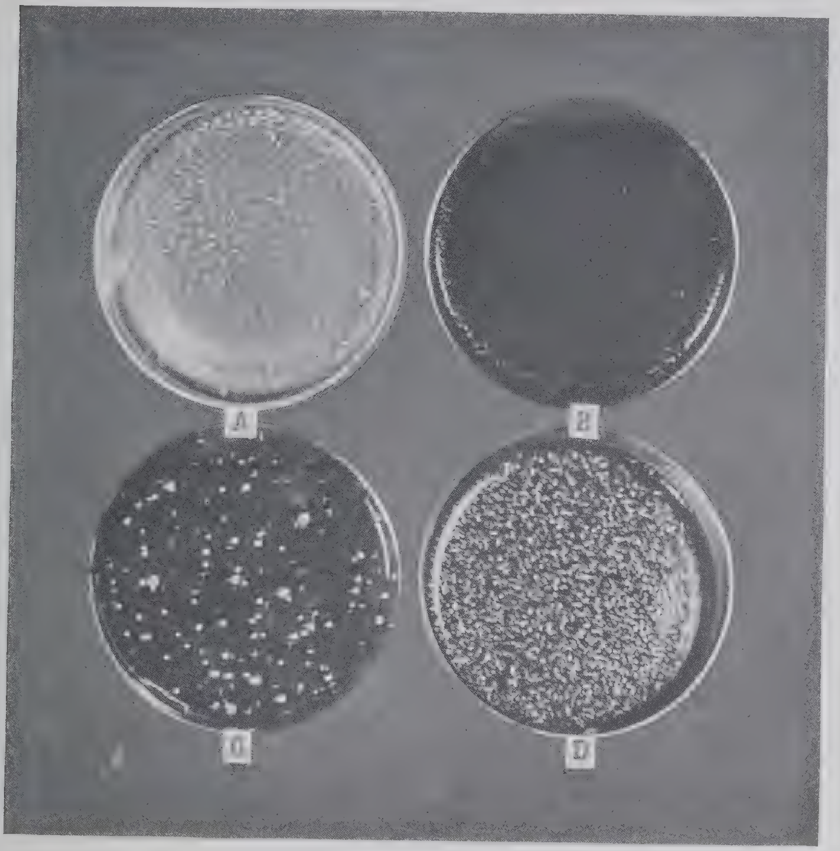


FIGURE 254. A TEST FOR BACTERICIDAL CAPACITY OF BLOOD OF A PATIENT WITH OSTEOMYELITIS. A, ONE THOUSAND LIVE ORGANISMS; B, ORGANISMS IN BLOOD FOR TEN MINUTES, NEARLY ALL DEVITALIZED; C, VACCINATION OF BLOOD WITH ONE HUNDRED DEAD, REDUCED EFFICIENCY; AND D, VACCINATED WITH ONE THOUSAND DEAD, DESTROYED DEFENSE.

addition of one hundred of these per cubic centimeter distinctly decreased its efficiency, and the addition of one thousand dead organisms almost paralyzed its bactericidal property. This patient was being stimulated to the limit of the capacity of his blood to react. The building up of his defense, as indicated by a chemical analysis of his blood, quickly reversed the trend of the battle and he gained twelve and one-half pounds in eight days' time. His case is studied in the chapter on Acid-Alkali Balance.

In our vaccines, we have found that in accordance with the suggestion of Douglas[25] that residual vaccines have in many instances apparently distinct advantage over those made in the usual way. Later work by Dreyer[26] has carried the previous work of Douglas farther, and has shown that the quality of acid fastness and Gram-positive reaction obtains in organisms because of the presence in their bodies of a fatty substance probably constituting a capsule, which lipoid substance is an armor for the unit bacterium against the chemicals furnished by the host in attacking these bacteria. This substance also acts as a retaining membrane to prevent the toxic substance leaving the organism, which becomes the antigen for calling forth the antibody that is constructed by the host. If, then, such organisms be used for vaccines, their potency is very low because of this encapsulation and retention. The subjecting of these organisms to a process of extraction of these lipoidal substances, removes the defensive mechanism from the organisms, and the vaccine made from this residuum has, as we have shown in other chapters, a very marked increase in efficiency. This holds promise, with higher development and perfection, of becoming a means for the benefiting of many individuals for whom vaccines have heretofore been unavailing. It is a matter of importance in looking over our records that the individuals for whom our vaccines have been less helpful, have had as their infecting organism, a Gram-positive strain. Such a case is the one referred to in the preceding paragraphs of this chapter, with the recurring bacteremia, also discussed in the chapter on Circulatory System.

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[25] See bibliography.
[26] See bibliography.

One of Nature's chief mechanisms in dealing with bacterial invasion has been shown to be a process of digestion by means of ferments probably supplied for the blood by the leucocytes. When organisms carry a large enough percentage of lipoid substances, they seem to be able to resist the action of these digestive ferments. This digestion process seems to be necessary for the liberation of the antigen, which, by its presence, will call forth the development of antibody suitable for its neutralization; and since it is the specific antigen of the organisms involved, or sufficiently similar to call forth this special ferment, that antigen is more or less specific for the organism involved. If, then, as has been shown by Dreyer and Douglas, the organism is predigested, for which purpose they use trypsin, the product so prepared is relatively very much more efficacious in stimulating the defense of the host. We have here, then, a means for greatly improving the efficiency of autogenous vaccines. The practical application of this is illustrated in the chapters on clinical applications.

SUMMARY AND CONCLUSIONS.

We would, accordingly, summarize:

1. The blood of individuals may be reinforced by the use of vaccines, and the type of vaccine, which will be helpful, can be determined in advance by studies of the blood *in vitro.*

2. Vaccines made from organisms from which the lipoids have been extracted not only are freer from the toxic substance which produces the undesirable reactions in the patient, but have the antigen set free and therefore available for calling forth the antibody within the body of the host.

3. Vaccines containing predigested organisms, from which the lipoid substances have been extracted, have qualities which enable them to stimulate the defensive mechanisms of the host, not obtained from vaccines made from organisms without these treatments.

In some individuals a low defense may be materially strengthened by the use of vaccines and also by the use of all available means for stimulating metabolism and increasing a supply of essential nutritional factors.

CHAPTER XLIII.

CALCIUM AND ACID-ALKALI BALANCE.

PROBLEM: What is the role of calcium in the maintenance of the acid-alkali balance of the blood, other body fluids, and tissues?

EXERIMENTAL AND DISCUSSION.

Calcium enters into the structure of most of the tissues of the body, being the chief constituent of the skeleton. This, however, is not its most important role, since every form of life, from the unicellular protozoa to the multicellular vertebrate forms, is dependent upon the presence of calcium ions for metabolism and function. Similarly, every cell of the body and of every plant is dependent upon calcium ions in both its cytoplasm and the fluids surrounding it.

The present current interpretations of dental pathology are filled with paradoxes, many, if not most, of which are directly or indirectly related to calcium. But these paradoxes have not been readily cleared up by the work of the preceding chapters, for, indeed, many new ones have, apparently, been added, such, for example, as the following: Why do we have the wasting of bone, as in periodontoclasia, and apical absorption present in those individuals who have high ionic calcium, for we should expect that they would be the ones that could furnish ionic calcium for deposition in the bone; and, conversely, why do we find condensing osteitis and lack of absorption in the presence of an irritant in those individuals who have a low ionic calcium; for, if any individuals could surely ill afford to deposit bone in excess, it would be those having an already depleted ionic calcium of the blood?

What could be a more simple and satisfactory explanation for rheumatism and deforming arthritis than one providing that an abnormally high ionic calcium of the blood produces, in the presence of an inflammatory irritation, a deposition in the inflamed tissue; and, conversely, that in the presence of an inflammation due to an infective process, an abnormally low ionic calcium would cause a removal from the bone of part of its structure? The above would be a very convenient hypothesis, since in the majority of instances of deforming arthritis in the acute processes the individual has a lower than normal ionic calcium of the blood. That such a line of reasoning is not based on fact is demonstrated in many ways, one of which is that in certain types of arthritis—namely, the degenerative type—as has been shown, the ionic calcium of the blood is higher than normal, and yet to the casual observer, both types would present symptoms that would seem to be similar and would frequently be classified as identical. It, therefore, cannot be true that the ionic calcium is in itself, by its presence or absence, the causative factor. When, however, we analyze these types of arthritis, we note that with the form which is accompanied by a higher than normal ionic calcium, there is a tendency to radiolucency of the bones, with distinct softening and wastage of the calcium; and, conversely, the proliferative type of arthritis, which is accompanied by the lower than normal ionic calcium, tends to have condensation of the bone. We have, then, in these two relationships comparable conditions to those which obtained in periodontoclasia, periapical rarefying osteitis, and osteomyelitis on one hand, and the absence of periodontoclasia, the absence of apical absorption, and tendency to condensing osteitis on the other hand.

It is apparent, then, that our calcium is playing a fundamental role and our fundamental problem is to determine what that role may be. If we return to researches that I have reported on periodontoclasia, alveolitis, rarefying osteitis, etc., we will readily see that the processes which result in the tearing down of alveolar bone have direct relationship to the presence of an irritant, but not only an irritant, an irritant plus toxic product from bacterial invasion. It is not the presence alone of either, however, the irritant or the bacterial infection, that is fundamentally and exclusively the etiological factor in periodontoclasia, for if the irritant be permitted to remain and bacterial growth be reduced to a minimum, the process largely terminates; and, conversely, if the mechanical irritant be removed, in many cases the bacterial invasion reduces or disappears and the process ceases. I have also noted that the content of the periodontoclasia pockets becomes more alkaline as we go more deeply into the acutely infected pockets. It is quite easy to understand how the ionic calcium of the saliva can reach 7.4, since that is the concentration of the H ions of the blood and from which there can be but slight deviation in health or disease. But it is not so easily explained how the stream can be higher than its source, for the pH of practically all periodontoclasia pockets will be at or above 7.4, and therefore above the pH of the blood of the individual in question. Again, as I have shown, sockets of extracted teeth which are making a rapid repair have a pH at or above 7.4, whereas those with a pH below that point are progressively slower in repair in proportion as the hydrogen ion concentration is depressed. It is also significant that the saliva of individuals with a tendency to periodontoclasia will be found to have a mien alkalinity above that of individuals without that tendency. A determination of the hydrogen ion concentration of the pus from flowing fistulae has revealed that it, too, is above that of the blood if the patient is making a winning fight. In our rabbits, however, in which a tooth is planted beneath the skin, the hydrogen ion concentration of the fluid about the infected tooth was found to have depressed to about 6.8 in those rabbits that were not making a winning fight, and always at or below that point at the time that the infection was causing the death of the rabbit.

Before discussing the experiments that I have set up for throwing further light on this question, I will review some of the characteristics of the blood itself. As previously stated, its hydrogen ion concentration (which is true of practically all the fluids which bathe tissue cells), remains practically constant at 7.4, and relatively large amounts of additions of either acid or alkali to blood will not considerably change it from this constant, whereas the same amounts added to water would produce a very considerable change. We are indebted to Henderson for the working out of the physicochemical bases of this phenomenon. He and others have shown this to be due to a very elaborate buffer system which is based upon the fact, that carbonic acid and other weak acids, like phosphoric, possess the remarkable quality of being able to maintain a constant reaction when there is present in the solution, which contains them, an excess of their salts. In the process of metabolism large quantities of carbonic acid are given off and combine directly with bases, such as sodium, to form sodium carbonate and bicarbonate, with the result that the balance is maintained between the ions of the carbonic acid and the sodium carbonate, with a constant reserve of sodium bicarbonate in the blood. The CO_2 is given off as gas in the lungs, leaving water, which continually and naturally takes care of the elimination of the excess acid. In the consumption of foods and their reduction to sugars and fats, and the final oxidation of these products, there is a progressive burning of the carbon by uniting with oxygen, with the production of heat which maintains the body temperature and which leaves the body normally as CO_2 from the lungs. The proteins of the body enter into the process and may act as either acids or bases since they are amphoteric. Each protein has its own iso-electric point, which is the point of its minimum electrical conductivity and the point at which the H ions and OH ions balance. This iso-electric point need not be, and, in fact, with proteins does not correspond with the neutrality point of water, but with many proteins is far on the acid side of neutrality.

In the process of metabolism, the nitrogen of the protein passes by way of the splitting of the protein into the amino-acids through several cleavage processes and is in the normal individual eliminated from the body almost entirely as urea, an end product. In disturbed metabolism part of the nitrogen may be eliminated as ammonia. If, therefore, the food that is consumed is most efficiently utilized by the body, all its potential energy will be represented in the various physiological processes as heat production, work, growth, secretions, etc., and can only leave the body in the form of completely oxidized and therefore energy-free end products, which end products are carbonic acid gas, urea, and water.

This, however, presupposes an ideal efficiency on the part of the functioning of the body. It is, however, quite impossible for the quantity of intake of food to be so exactly controlled, or for the working mechanisms to be in such perfect condition as to provide for this ideal metabolism. If, in the utilization of the sugars, which is Nature's form of storing up the energy-producing products, there is not complete oxidation in these progressive stages, acids of larger molecular structure than carbonic acid will be formed; and since it is the only acid that will be eliminated as a gas, these others cannot be gotten rid of in so simple a form as is that acid, and they must, therefore, be neutralized. Such incomplete oxidation products are present as acetoacetic acid and butyric acid. The neutralization of these acids can only be accomplished by the use of bases which are present in the body. The most economical and available of these will be ammonia, and they will accordingly be eliminated as ammonium salts in the urine. When, however, the base ammonium is not available for this neutralization process, since it must be accomplished at

RELATION OF ALKALINITY INDEX TO CALCIUM

Case No.	Rab-bit No.	Date	Days After 1st Injec-tion	Alkalinity Index		Calcium Ionic		Calcium Combined	
				Injection		Injection		Injection	
				Before	After	Before	After	Before	After
1422	1217	7– 9–23		Imp. 45.70	Imp.	10.067		2.808	
		7–10–23	1		51.40		9.24		3.982
		7–11–23	2		51.30		7.627		2.840
		7–12–23	3		44.90		9.24		0.72
1422	1242	7– 9–23		Int-v 43.40	Int-v	8.00		2.067	
		7–10–23	1		48.40		8.128		1.112
		7–11–23	2		52.30		7.354		0.984
		7–12–23	3		50.48		7.658		1.598
		7–13–23	4		54.20		8.012		1.885
		7–16–23	7		49.13		8.857		1.728
1317	1247	7–17–23		Imp. 38.10	Imp.	8.714		2.714	
		7–17–23	½		39.10		8.714		3.894
		7–18–23	1		37.12		8.671		2.910
		7–20–23	3		44.22		9.600		2.400
		7–24–23	7		44.44		9.440		4.340
1414	1230	6–12–23		Int-v 37.85	Int-v	9.045		0.585	
		6–15–23	3				9.24		2.965
		6–16–23	4		52.40				
		7–30–23	48		27.46				
1414	1232	6–12–23		Int-v 44.25	Int-v	9.72		3.242	
		6–14–23	2				8.313		1.567
		6–16–23	4		54.45		7.727		
		6–18–23	6				8.016		2.919
		6–28–23	16		42.31				
1409	1248	7–19–23		Imp. 38.72	Imp.	10.17		1.578	
		7–20–23	1		36.88		10.60		0.534
		7–24–23	5		44.10		9.24		1.160
1409	1250	7–19–23		Imp. 32.68	Imp.	9.45		1.096	
		7–20–23	1		36.88		9.40		0.520
		7–24–23	5		44.04		9.04		2.96
1414	1234	6–12–23		Int-v 37.40	Int-v	9.45		0.180	
		7– 3–23	21		26.10				
1426	1251	7–20–23		Imp. 39.90	Imp.	8.96		0.20	
		7–26–23	6		45.90		9.26		1.085
		7–26–23	6		24.47				
1414	1235	6–12–23		Int-v 43.00	Int-v	9.640		0.320	
		7–30–23	48		30.05				
1424	1252	7–23–23		Imp. 40.88	Imp.	11.134		1.474	
		7–26–23	3		40.80		10.82		1.321
1424	1255	7–24–23		Int-v 40.00	Int-v	9.16		0.43	
		7–27–23	3		40.42		9.04		0.80
		8– 1–23	6		39.50		9.321		1.241
1426	1249	7–20–23		Imp. 38.18	Imp.	9.40		0.44	
		7–26–23	6		40.90		9.56		0.985
		7–28–23	8		36.14				
Sick Rabbit from Stock					26.40				

Imp.—Implantation
Int-v—Intravenous

FIGURE 255.

any price, the body must use such other bases as are available for its accomplishment. A continual supply of such an abnormal acid in the blood, requiring immediate and complete neutralization, since the hydrogen ion concentration of the blood will always be maintained at 7.4, must result in a depletion of those chemicals which are held in reserve in the blood for the purpose of neutralizing such abnormal acid formations. The neutralizing value of the reserve system of buffers in any blood can be determined by chemical processes. One of these is to take some of the blood serum, never allowing it to be exposed to carbonic acid gas at any moment from the time it is drawn until the determinations are made, and determine the amount of carbon dioxide that will be neutralized by it before its pH will be changed. As this method is very exacting, simpler titration methods have been perfected which give very constant results, and we have used this latter method in these studies, particularly the method of Greenwald[27].

We have, accordingly, made quite a large series of determinations to ascertain the relationships which exist between depleted buffer systems and the various normal and pathological states in which we have found our patients. I have shown in previous chapters, and particularly in Chapter 20 on the Chemical Changes in the Blood, Produced by Dental Infections, that there is a marked tendency for patients with periodontoclasia (which we will now think of as a group characteristic and as representing a constitutional state,) to develop diabetes. I have also shown in the extensive table of Figure 131 of Chapter 20, that there is a marked tendency to the development of a decrease in the alkali reserve of these patients. This has suggested a careful study to determine to what extent dental infections enter into the disturbing of the mechanisms of control for these various balances and the production of acid substances, and, particularly, to determine to what extent the calcium of the body takes part in the maintenance of the normal hydrogen ion concentration of the blood by its use in the neutralization of pathological acidities.

As one means for determining this, we have made morphological and chemical analyses of the bloods of rabbits before and after inoculating them with dental cultures or the placing of an infected tooth beneath the skin, and also when subjecting them to the filtered toxins from extracted teeth. Some of these results are shown in Figure 255. One of the important indications is shown in the column in Alkalinity Index, in which it will be seen that rabbits starting with a normal alkali reserve—namely, an alkalinity index from 38 to 45—after being injected with a culture from an infected tooth or having one planted beneath the skin, had as one of their first effects a boosting of the alkalinity index to well above normal, which seems to be an important part of Nature's defensive reaction. When, however, these animals have become sufficiently involved to tax the defensive mechanism, this alkalinity index falls rapidly to and below normal and continues falling until they approach death. When we compare the alkalinity index column with the ionic calcium column, we find that similarly there is some tendency for the ionic calcium to go up slightly immediately following the invasion, and that as the ionic calcium goes down (which it practically always does) with the progressive overwhelming of the animal, there is a corresponding loss of alkali reserve. In other words, these animals have had established in their bodies a state of acidosis as a result of their heroic, and we should say effective, reaction in the combat against this infection.

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[27] See bibliography.

When we compare these data with the results disclosed in the chart in Figure 131 of Chapter 20, we find that the patients suffering from severe and continued infective processes frequently, if not generally, had reductions and some very marked reductions in the alkali reserve. Case No. 1311 was reduced to 23.3. When we apply this to a similar fight against an acute dental infection in our patients, we find a similar process in progress. Case No. 1417 had an acute osteomyelitis following the extraction of an abscessed central incisor. The roentgenographic view of the condition is shown in Figure 256, and it will be noted that the necrosis had extended to the first molar, involving the lateral cuspid and both bicuspids so severely that the second bicuspid had almost completely lost its attachment. In this case it will be seen that his alkali reserve was reduced to 26.6, nearly to half its normal. In other words, he was in a state of distinct acidosis. His ionic calcium was reduced, but most important, his pathologically combined ionic calcium was up to 3.35, a very unusually high reading. The treatment of his case consisted in placing him on bicarbonate of soda, to furnish to his blood a cheaper base with which to neutralize the pathological acids and relieve it of the overload which was being paid for partly in calcium. This man had lost twenty-five pounds in eleven days. He was also placed on a liberal intake of cal-

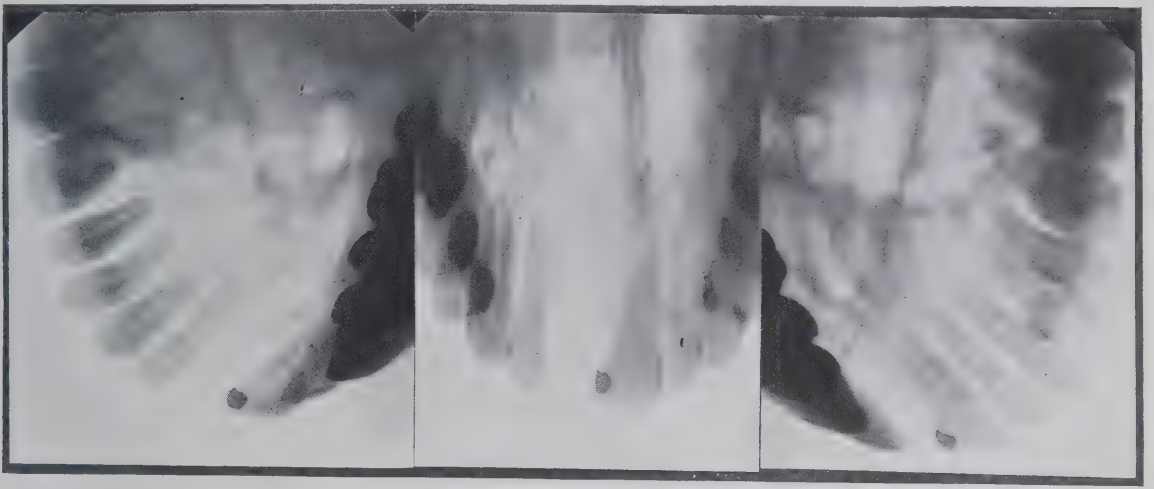

FIGURE 256. MAXILLARY OSTEOMYELITIS FOLLOWING APICAL ABSCESS.

RELATION OF CALCIUM TO ALKALINITY INDEX			
Day of Study	Ionic Calcium	Combined Calcium	Alkalinity Index
1	9.786	3.350	
3	9.785	2.857	26.60
4	10.534	1.136	25.00
7	9.045	1.235	34.70
15	9.84	1.336	30.15
23	10.935	1.405	34.68
29	10.142	1.422	30.16
36	10.314	.964	32.40
65	10.256	1.078	**41.36**

FIGURE 257.

This patient lost twenty-five pounds in eleven days during the activity of this case of osteomyelitis, and under treatment regained twenty-one pounds in a few weeks. Note that his alkalinity index progressed from the low point of 25 to 41, approximately normal.

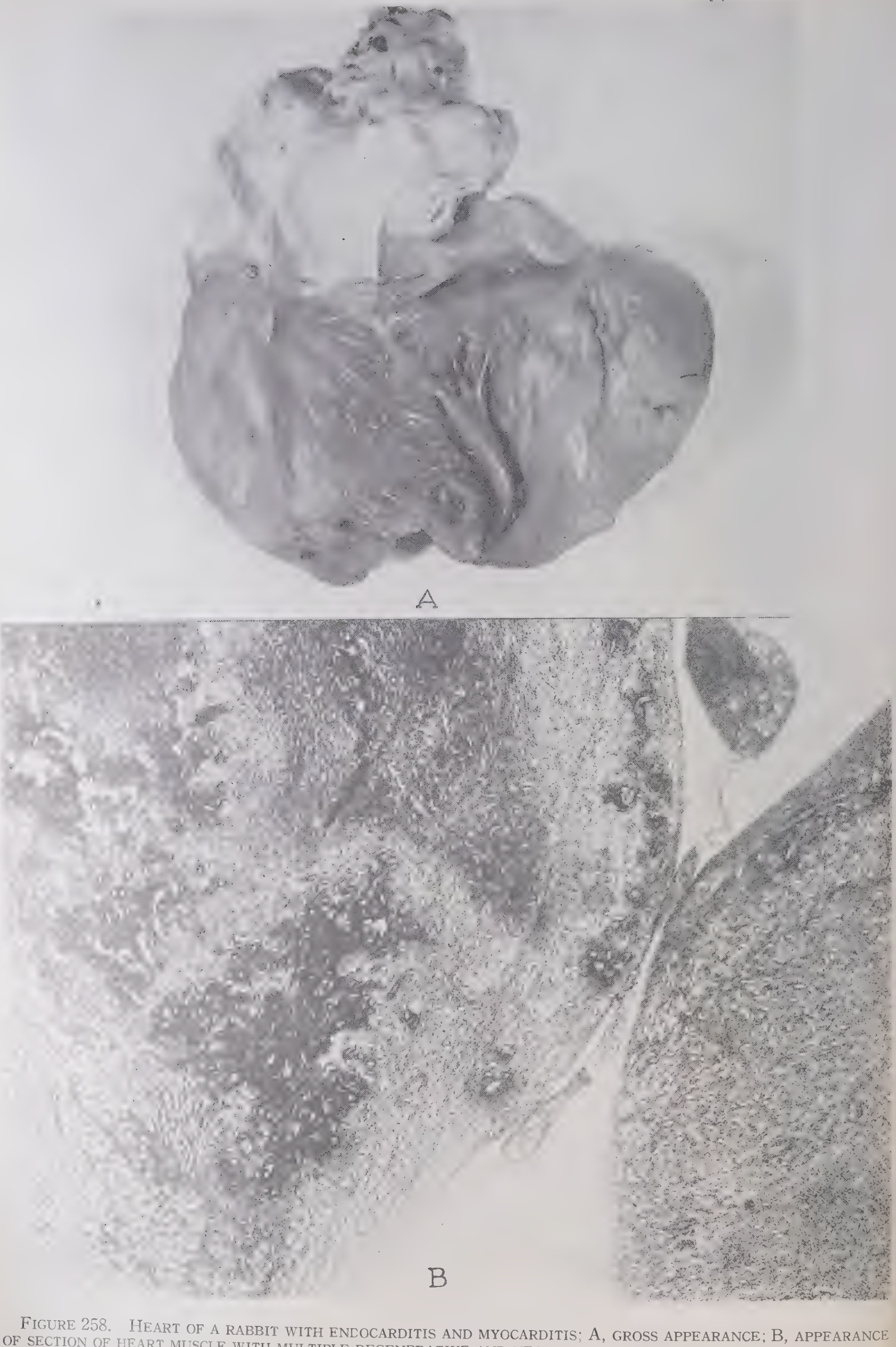

Figure 258. Heart of a rabbit with endocarditis and myocarditis; A, gross appearance; B, appearance of section of heart muscle with multiple degenerative and necrotic processes.

cium in the form of milk and calcium lactate and parathyroid to assist in the metabolism of the calcium. Results were most striking. His alkali reserve progressed rapidly toward normal, his lassitude and nervousness quite rapidly disappeared, the advancement of necrosis immediately ceased, and he gained thirteen and one-half pounds in about ten days. The relation of his ionic calcium and the pathologically combined calcium to the fluctuations in alkalinity index are shown in Figure 257. Note that, in general, as his alkalinity index went up, his ionic calcium increased and his pathologically combined calcium decreased. The condition that obtained was probably somewhat as follows: With the increase of his alkalinity index he was better able to fight the infection; with the decrease of the infection there was less toxic substance to combine with the ionic calcium to produce a pathologically combined calcium.

As a further means of study of this problem a rabbit (No. 1234) was inoculated with a culture from a patient suffering from neuritis, nervous breakdown, and heart involvement, and in twenty-one days the rabbit was chloroformed for study. One of the knees had developed a purulent arthritis and the heart had developed two major lesions, one a myocarditis with fibrosis, and the other granulation on the valve cusp, shown in Figure 258. While this rabbit was losing in weight, it was apparently not near death and yet its alkali reserve of the blood had been reduced to 25.

When we consider some of the clinical data regarding arthritic patients, we get a suggestion at once that this may be one of the important explanations for our inability to make progress with the ordinary method of treatment. This is illustrated in Case No. 1311, in which the alkali reserve was down to 23.3, and in which the ionic calcium was depressed. Under forced nutrition with milk, he was able to bring his ionic calcium up temporarily, but it did not tend to remain up without the continued pressure. The elimination of the dental infections, which were undoubtedly an important contributing factor in the development of this condition, had not been sufficient. Placing this patient on a vigorous treatment of bicarbonate as a means of testing to see whether his marked acidosis could be alleviated, if not materially improved, changed his alkali reserve to 36 in ten days' time. If our interpretation of his condition is correct, this procedure has made possible the neutralizing of abnormal acids with the artificially supplied base, sodium bicarbonate, and thereby relieving the system of the expensive process of neutralizing it with its most available base, a calcium compound. Whether or not this is the correct interpretation, his marked improvement indicates that the metabolic processes were directly affected.

It is impossible, as yet, to explain the role of the accessory food factors and of toxic substances in the disturbances of metabolism and catabolism. It is probable that the development of acidosis in connection with scurvy and beriberi have to do with an aberrant metabolism of carbohydrate in the absence of the particular vitamin responsible by its absence for those conditions. Hamilton[28] has shown the minimum amount of calcium required per day to neutralize the products of incomplete oxidation to be 200 mgs. for an infant. If we will put this on a per kilo basis and assume that the adult requires a proportionate amount, it will readily be seen that a gram or more of calcium may be required per day. Sherman has shown a minimum daily need of the normal adult to be about six-tenths of a gram. If, however, an individual is suffering from an acidosis for which his body has not been able to make an adjustment by the establishing of a compensated acidosis, such as the neutralizing of the acid products with a base the body can spare, the demand for such expensive bases as calcium may become very great, and the amount required may be much more than the minimum above estimated. In health the sources of calcium will be mainly from the blood stream, which reservoir will be constantly replenished with food, provided that not only the laws of supply and demand shall balance, but provided the mechanisms which control calcium metabolism are in such adjustment that the balance may be and is, ordinarily, maintained. The mechanisms of control of calcium metabolism are as yet but little understood and of necessity must be very complicated. If we will take as an illustration the infinitely small amount of the activating substance that must be present to make possible the utilization for metabolic processes of the sugar of the blood, and which product is manufactured by the islets of Langerhans of the pancreas, the quantity is so amazingly small that it is almost beyond conception. To illustrate:

If the relatively concentrated product that is secured by the successive purifications of insulin is injected into a normal rabbit, a one four-thousandth of a gram is sufficient to reduce the normal sugar of the rabbit's blood from about 100 mgs. per 100 cc., to or below 40 mgs., by a process which is probably one of metabolism of the sugar, and the rabbit will go into convulsions which will end in death. If, however, there be injected into the rabbit's circulation a small quantity of sugar, it is almost instantly made normal.

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[28] See bibliography.

In the pathological state of diabetes it is the inability of the body to metabolize sugar which it makes from the carbohydrates, due to the absence of this chemical. When we realize, then, that so simple a substance as sugar, Nature's principal fuel within the body, is not available except with the aid of insulin furnished by the pancreas, we see how easily it might be that even calcium metabolism may similarly be dependent upon some such delicately balanced hormone or vitamin. In the chapter on Glands of Internal Secretion, I have discussed the role of the parathyroids in this relation. If, then, we will undertake to visualize what seems to be one of the considerations in connection with calcium metabolism, it might be presented as follows:

The heat is necessary in the cold winter to keep the house warm. The fuel of choice and that we may plan to burn, may be coal. If we cannot get coal to unite with the oxygen for combustion to make the necessary heat, we may utilize wood. This wood may come from the wood yard, a base of supplies for firewood. If, however, that base gives out, the furniture of the house may be burned. Even this may not endanger life; but when the furniture is almost burned, it may be necessary to take off some of the doors and burn them for the heat of combustion for the protection of life. But the burning up of the doors and floors of the house destroys the house. It cannot function without them.

If, then, we will think of the skeleton of the body as a storehouse for calcium, just as the dwelling is a storehouse for wood, not for the purpose of having it available for fire but as the framework of the edifice, under normal conditions Nature does not require to draw upon the framework of the dwelling—namely, the skeleton—for a base with which to neutralize invading acids, the products largely of incomplete oxidation and often in part resulting from overwhelming the body with unnecessary and undesirable foods. If these substances are not oxidized and neutralized, they may accumulate in the body. If they are oxidized at the expense of fundamental bases, such as calcium, because no other product is made available by the system, the first disturbance will express itself probably in the circulating ionic calcium of the blood. There is a limit at which the body will permit this source to be overdrawn. When that limit is reached, the calcium must be taken from the framework—namely, the skeleton—in order to pay the bills. If this process is associated with a balanced mechanism that is very sensitive to the maintenance of a compensated acidosis—that is, a constitution that sees to it that all bills are paid promptly—the individual will have the capacity for a high defense until that time comes when the available supply is not adequate, and quite unexpectedly and all too frequently we see those individuals developing some of the many types of acidosis, one of which is associated with diabetes. This capacity for paying the bills promptly not only makes the individual relatively safe against infections and invasions during the period of his ample defense, but means that in any local tissue where the body mechanisms cannot maintain this neutralization, the bills will be paid from the local storage; and if this process is part of the warfare resulting from a bacterial invasion which has developed about a mechanical irritant, such as an impinging gold crown, an irritating margin of a filling, of a food pack between the teeth, that warfare against the local toxic substance will be consummated at any cost, a part of which is the sacrificing of the alveolar bone and hence alveolitis, or periodontoclasia or pyorrhea alveolaris. If the warfare is at a root apex instead of a gingival margin, the bills will be paid in the same coin. We therefore see, if this is a part of the process, why it is that either the removal of the irritant or the removal of the toxic invading process, will cure the pyorrhea so-called. We also see why the individual who does not make this type of reaction, who does not have the capacity to pay the bill at any price, does not have this type of local expression. If, however, this individual's defense is not normally high against streptococcal infection, and he has developed a focus from which toxin and bacterial products are passing throughout his body, local zones of irritation will be established. If these occur in joints or in relation to hard structures, there may be either the tearing down of bone, or the deposition of bone, or both, just in accordance with the balance of these two forces expressing themselves in degeneration and proliferation.

The question of what becomes of the calcium and how a patient may be examined to see whether a sufficient quantity be present either in the body or blood stream for the various metabolic processes, is a most important one. It is, however, complicated by many difficulties. In the first place, any analysis based, for example, on an incineration method, while giving the total calcium in the material being examined, throws no light whatever upon its availability for a particular use within the body, and this does not apply only to the calcified structures, for a blood with a high pathological quantity of combined calcium may, by an incineration method of calcium determination, show a normal or high blood calcium while in fact the available ionic calcium of the blood may be dangerously low. Nor will an examination of the various sera of the body show whether the calcium is being retained because of defective metabolism or elimination unless that same determination identifies the calcium structure present as being in the proper physical and chemical state which those conditions require. The calcium that is used up in body metabolism is eliminated in the feces as a calcium soap and may be considered as an end product and not available again for service within the body. The problem is therefore a most difficult one because of its many involvements. The details of calcium metabolism are not yet sufficiently known to establish what form the calcium actually takes in various of the metabolic processes.

SUMMARY AND CONCLUSIONS.

I would therefore summarize:

1. The researches recorded in this and the preceding chapters strongly suggest that one of the roles of calcium is defensive in the neutralization of products of incomplete oxidation, which are not normally present in the bodies of normal individuals, and which, when they do develop, should be neutralized by bases less costly to the body.

2. Dental infections tend to produce injury, either by disturbances of the mechanisms which control calcium metabolism or by the production of toxic substances which directly or indirectly cause the development of acid substances in the system, the presence of which depresses or inhibits normal processes of metabolism and catabolism.

I would, accordingly, express my conclusion as follows:

> **In the proper functioning of the body, the end products of metabolism are carbon dioxide, urea, and water. When metabolic functions are abnormal, resulting in the imperfect oxidation with the development of less simple acids than carbonic acid, these must be neutralized with bases taken from the body and its fluids. In the absence of an**

adequate supply of these from other sources, the demand must be met by the calcium of the body, first from the circulating ionic calcium, then from the calcified tissues. This latter is the characteristic end reaction involved in periodontoclasia, or pyorrhea alveolaris. This enters into and complicates the etiology of many, if not most, of the rheumatic group disturbances studied in detail in subsequent chapters.

See bibliography references 29, 30, 31, 32, 33, 34, 35, 36, and 37.

CHAPTER XLIV.

DENTAL INFECTIONS AND TISSUE AND ORGAN DEGENERATION.

PROBLEM: To what extent and in what manner do dental infections contribute directly and indirectly to the degeneration of tissues and organs of the body and to disfunction of the same?

EXPERIMENTAL AND DISCUSSION.

In the preceding chapters we have studied many phases of the relation of dental infections to vital processes. In many of these we have compared, in a more or less quantitative way, the pathological states of patients. In Chapter 20, on Chemical Changes in the Blood Produced by Dental Infections, I have shown many instances of parallelism between the pathological states of the patients, as expressed serologically, with those produced in rabbits and rats that had been subjected to either the inoculations with dental cultures or planting of infected teeth beneath the skin. In Figure 131 of that chapter I have given approximately one hundred successive analyses of the blood, and related them to the dental pathology and systemic conditions of the patients. These reveal many instances of important associations, as, for example, a high ionic calcium of the blood with periodontoclasia, and of both high ionic calcium of the blood and periodontoclasia with hyperglycemia and glycosuria. Similarly, it was shown that with the development of extensive toxic disturbance from dental infection, patients tended to have reduction of the ionic calcium of the blood with an increase of a pathologically combined calcium of blood, which condition was practically universally produced also in experimental animals, whether they were inoculated intravenously with a strain taken from a dental source or whether a tooth was planted beneath the skin of the experimental animal.

Data were presented which seemed to demonstrate that a disturbance of carbohydrate metabolism when it exists in patients, as in diabetes mellitus, may be influenced by the removal of dental infections, and, similarly, changes in the blood sugar of experimental animals could be produced with dental cultures, amounting to a distinct hyperglycemia. In the chapter on Glands of Internal Secretion the researches reported seemed to establish that dental infections may very definitely disturb the functioning of these various structures, especially that of the thyroid and pancreas. In the chapter on Elective Localization of Bacteria of Dental Origin, the data developed by the researches reported seem to establish, as has the work of several others, that dental infections have a direct relation to, and are important contributing factors in, the establishment of infective processes in various organs and tissues of the body. While these various studies strongly indicate that there is a distinct responsibility on the part of dental infections in the production of degenerative processes in the organs and tissues, the data presented do not make sufficiently clear the fundamental nature of the process involved. This research has therefore been undertaken to establish, if possible, more exactly the nature of these processes.

In Chapter 41, in studying the defensive mechanisms of the blood, many important new data were presented, which established in further detail the role of the leucocytes and the fact, that they are under certain conditions paralyzed by dental infections and probably by the toxins from infected teeth. In Chapter 43 we have seen how calcium may be taken from the circulation to neutralize products of incomplete oxidation in the absence of some other base less costly to the patient than the calcium. Since a freshly extracted infected tooth, when placed in defibrinated blood or blood serum, will in many instances very greatly reduce the ionic calcium of that blood and, which may accordingly be present and measurable as a pathologically combined calcium, may it not be that this toxic substance may have a direct relation to either the more gross factors involved in metabolism, or, more important, be directly related with the governing factors controlling the detailed processes of metabolism and catabolism? We might, therefore, restate our problem: What are the relations of the products of dental infections to processes of metabolism and catabolism and to the organs and tissues engaged therein?

As one method of approach to this problem I have had studies made to observe the changes in the alkalinity index, or so-called alkali reserve, of the blood. Before proceeding with this discus-

ALKALINITY INDEX OF BLOOD OF PATIENTS

Case No.	Alkalinity Index	Dental Symptoms	Systemic Symptoms
1311	**23.30**	Slight Locked Apical	Rheumatic Arthritis
1337	**39.40**	Several Locked Apical	Enlarged Cervical Glands and Lassitude
1325	**42.37**	Periodontoclasia	Rheumatism
1339	**39.50**	Locked Apical	Neuritis
410	**34.4**	Periodontoclasia	Normal
1346	**47.20**	Chronic Periodontoclasia	Normal, after illness
1409	**31.8**	Locked Apical and Periodontoclasia	Lassitude
1332	**46.0**	Slight Locked Apical	Normal
1359	**41.0**	Locked Apical	Nervousness
1363	**36.14**	Locked Apical	Rheumatism and Nervousness
1416	**38.65**	Periodontoclasia	Degenerative Arthritis
1417	**26.60**	Suppurative Necrosis	Osteomyelitis
987	**32.50**	Normal	Rheumatism and Heart
335	**32.53**	Normal	Bursitis and Lassitude
1421	**39.39**	Periodontoclasia	Near Normal
1419	**25.49**	Locked Apical	Lassitude and Hypertension
1324	**20.36**	Periodontoclasia	Osteomalacia
1425	**27.16**	Locked Apical	Nephritis
1381	**23.00**	Chronic Ulcers	Normal
1423	**34.24**	Apical and Gingival	Hyperthyroidism
1381	**32.22**	Normal	Lassitude
1417	**31.20**	Suppurative Necrosis	Osteomyelitis
1311	**33.94**	Normal	Deforming Arthritis
1427	**25.90**	Periodontoclasia	Tuberculosis
1428	**24.20**	Periodontoclasia	Tuberculosis
410	**25.30**	Chronic Periodontoclasia	Periostitis and Lassitude
425	**29.63**	Locked Apical	Digestive Trouble
2168	**23.76**	Periodontoclasia	Diabetes

FIGURE 259.

ACID-BASE RELATION TO SYMPTOMS AND TREATMENT. CASE NO. 1417

Day of Study	Ionic Calcium	Combined Calcium	Alkalinity Index	Urine		Weight	Gain	Loss	*Systemic Treatment
				pH A.M.	pH P.M.				
1	9.786	3.350				133¾			
2									Systemic Nos. 1, 2, 3
3	9.785	2.857	26.60						
4	10.534	1.136	25.00	5.52		133½		½	Continued Nos. 1, 2, No. 3, 10 grs.
7	9.045	1.235	34.70						Continued all
11						136½	2¾		Continued all
12						137¼	3½		Continued all
13						138	4¼		Continued all
15	9.84	1.336	30.15	5.39		138¾	5		Continued all
16				6.59		138		¾	Continued all
18				4.98		140¼	6½		All discontinued by me.
20				5.14	4.99	140		¼	All discontinued by me
21				4.99	5.14				All discontinued by me
22				3.96	4.24	139		1	All discontinued by me
23	10.935	1.405	34.68	4.18	4.87	141	7¼		Resumed No. 1, 2 No. 3, 15 grs.
25				5.42	6.62	140		1	Continued All
27				5.39	6.53	140	6¼		Continued All
29	10.142	1.422	30.16	4.28	4.51	141	7¼		Patient neglected No. 3.
30				6.03	6.84				Resumed All
31				6.65	6.95	142½	8¾		Continued All
32				6.76	7.23	143¼	9½		Continued All
33				6.23	7.75				Continued All
34				7.33	7.84				Reduced No. 3 to 5 grs.
36	10.314	0.964	32.40	6.96	6.98	145½	11¾		Reduced No. 3 to 5 grs.
65	10.256	1.078	41.36	5.63	5.97	145	11¼		Discontinued all

*Systemic Treatments.
No. 1—Parathyroid 0.1 grain daily.
No. 2—Calcium Lactate 5 grains 3 times daily.
No. 3—Bicarbonate of Soda 5 grains half hourly.

FIGURE 260.

sion it is desirable to call attention to the fact, that there is strong opposition to the use of the term "Alkaline Reserve" because the term presupposes that in addition to the alkali that is held in combination, there is a quantity stored up available for sudden demands, but which, while in storage, is taking no part in the process of metabolism. Haldane and others have shown (British Medical Journal, April 9, 1921) that in cases where the blood is abnormally alkaline, the actual alkaline reserve may be diminished, and, conversely, that it may actually be increased in cases where the blood is deficient in alkalinity. He shows how that in actual fact the whole of the normal alkaline reserve is required to balance the carbonic acid normally present. Macleod has shown how in many cases (Physiology and Biochemistry in Modern Medicine) that there may be a compensated acidosis or a compensated alkalosis. In our studies of patients with degenerative processes of the various rheumatic group lesion types we have found a great divergence in the alkalinity index of the blood. In Figure 259 will be seen a group of twenty-eight successive individuals, and it will be noted that the variation runs from 47.2, approximately normal, to 20.3. When, however, we compare the physical condition of these various patients with this alkalinity index, we find immediately that the individuals in the most serious condition have the lowest alkalinity indices; whereas, those normal, or approximately normal, have an approximately normal index.

Case No. 1417 has had an osteomyelitis which has been checked very quickly by the administration of sodium bicarbonate, together with the administration of parathyroid, one-tenth grain daily, and calcium lactate, fifteen grains three times a day; and this patient who lost twenty-five pounds in a couple of weeks' time during the suppurative process, gained eighteen and a half of it back in about two weeks' time after being placed on this treatment. Notwithstanding the fact, that he was receiving fifteen grains of bicarbonate every half hour during the day, at least was supposed to get this amount, his urine did not become alkaline. To check the relationship of these conditions more exactly to the neutralization of acid products within his system, the bicarbonate and all treatment was stopped, with the result that he lost in weight, the suppurative process increased, and his urine quickly became strongly acid. He was placed back on the bicarbonate, parathyroid, and calcium treatment, and in twenty-four hours there was a distinct improvement which was marked in forty-eight hours. When asked what the particular differences were that he could recognize in his feelings, he said that when he was taking the medicine he felt rested when it was time to get up and wakened up fully awake; whereas, when he was not taking the medicine, he did not feel rested from his sleep.

In Figure 260 we see in parallel columns the ionic calcium, the combined calcium, the alkalinity index, the treatment, and change of weight of this patient. It will, accordingly, be seen that we have here a very strong indication that a disturbance of the acid-base balance is an important factor in his pathological state. When we review the history of his case, we find that he had a neglected gingival infection. An acutely abscessed tooth was extracted. The socket became infected from his gingival infection, for the spirochetes were found deep in the necrotic bone though his chief infection was streptococcal. His acute apical infection lowered his general defense so suddenly and severely that he apparently became a prey to the spirochetal and mixed infection of the gingivæ, which still more rapidly overwhelmed him. Fig. 260 also shows the pH of the urine.

In order further to check the effect of dental infection, I have had placed infected teeth beneath the skins of rabbits in order that we might compare the morphological changes in the blood, the ionic calcium, combined calcium, and alkalinity index. A group of these are shown in Figure 261. In rabbit 1234 it will be noted that at the time of death the polymorphonuclears had dropped to the very low count of 13.3 and the small lymphocytes had increased to 81.6. The ionic calcium had fallen from 9.4 to 7; the pathologically combined had increased from 0.18 to 2.83, and at death was at 1.52. The alkalinity index of this rabbit was 37.4, slightly below normal, when the experiment was started, and decreased to 26.1. This rabbit was chloroformed twenty-one days after being inoculated with the dental culture from a patient suffering from heart involvement and neuritis, and this rabbit had endocarditis, myocarditis, and joint involvement. Rabbit 1217 died in three days after the planting of a tooth, and it will be seen that the chief effect was an increase of the alkalinity index. This will be discussed later. Its polymorphonuclears decreased and its small lymphocytes increased. The ionic calcium dropped from 10 to 7.6. We have, therefore, in the second rabbit, a quite different reaction from that in 1234. When we take a number of terminal readings on rabbits with

Case No.	Rabbit No.	Days After	Alkalinity Index		Calcium Ionic		Calcium Combined		Weight			Days Lived	Blood Count			Remarks
			Before	After	Before	After	Before	After	Per Day	% Loss	% Gain		Whites	Polys	Small	
A1422	1217	Imp.	**45.7**		**10.0**		2.80		1419				9,600	37.5	50.0	Emaciation, congestion of heart.
		1		**51.4**		**9.24**		3.98	1387				6,800	45.0	50.0	
		2		**51.3**		**7.62**		2.84	1325				7,600	31.5	62.9	
		3		**44.9**		**9.24**		0.72	1289	9		3				
A1414	1234	Intv.	**37.4**		**9.45**		0.18		1219				7,400	13.3	81.6	Chloroformed. Endocarditis and Myocarditis, right knee arthritic.
		21		**26.1**					1197	2		21				
A1426	1251	Imp.	**39.9**		**8.96**		0.20		995				10,800	46.6	44.5	Emaciation, hyperemia, subcutaneous abscess.
		6		**45.9**		**9.26**		1.085	959				7,200	32.5	56.5	
		6		**24.4**					862	13		6	4,600	36.8	52.6	
B1317	1247	Imp.	**38.1**		**8.71**		2.71		1165				14,200	28.3	62.3	General condition good. Locally large hard swelling at site of implantation.
				39.1		**8.71**		3.89	1146				10,500	21.0	65.0	
		1		**37.1**		**8.67**		2.91	1176		1		9,800	28.0	63.1	
		3		**44.2**		**9.60**		2.40	1162				18,800	63.6	31.8	
		7		**44.4**		**9.44**		4.34	1129	3			18,300			
B1414	1232	Intv.	**44.2**		**9.72**		3.34		1145							Paralysis, and emaciation. Very alert.
		2				**8.31**		1.56								
		4		**54.4**		**7.72**			1072				12,900	39.3	49.1	
		6				**8.01**		2.91	1079				9,200	37.6	56.7	
		16		**42.3**					1015	11			14,500	43.4	45.3	
B1409	1248	Imp.	**38.7**		**10.17**		1.57		1322				17,200	35.0	34.7	Slightly emaciated. Small swelling. Very alert.
		1		**36.8**		**10.6**		0.53	1298				12,200	50.4	43.3	
		5		**44.1**		**9.24**		1.16	1279	3			16,000			
B1409	1250	Imp.	**32.6**		**9.45**		1.09		1302				12,800	36.5	56.0	No abnormal developments.
		1		**36.8**		**9.40**		0.52	1280							
		5		**44.0**		**9.04**		2.96	1263	2			4,000			
B1414	1235	Intv.	**43.0**		**9.64**		0.32		1335				18,000	58.3	34.6	General condition good.
		48		**30.0**					1437		17					
C1414	1230	Intv.	**37.8**		**9.04**		0.58		1324				9,100	30.0	60.0	Slightly emaciated, otherwise O. K.
		3				**9.24**		2.96	1285				15,000	27.0	69.0	
		4		**52.4**					1233							
		48		**27.4**					1490		11		14,200	37.7	56.6	
C1424	1252	Imp.	**40.8**		**11.13**		1.47		1959				14,200	26.3	63.1	Slightly emaciated, swelling on back.
		3		**40.8**		**10.82**		1.32	1912	2			16,400	19.5	68.0	
C1424	1255	Intv.	**40.0**		**9.16**		0.43		1254				10,700			Slightly emaciated, otherwise normal.
		3		**40.4**		**9.04**		0.80	1247	.6			17,000	70.6	20.6	

A—Killed by infection, or near death when chloroformed.
B—Making good defensive reaction.
C—Not injured by infection as yet.

FIGURE 261.

implanted teeth, we find that not infrequently the alkalinity index goes down to and below 25.

In Chapter 30, The Nature of Sensitization Reactions, I have shown the results of studies comparing the toxin of dental infections with histamine, and it was shown that there were some factors in common, one being the marked engorgement of the mesenteries, dilatation of the blood vessels of the small intestine, and one sensitized rabbit died within two minutes after receiving its infection. Further studies of this toxic substance indicated that it had some characteristics differing very distinctly from those of histamine. This suggested another approach to this problem.

On reviewing the various data of the preceding chapters, it has been disclosed that a very frequent effect of dental infections on both humans and experimental animals (when the latter had an infected tooth placed beneath the skin or were injected with a dental culture) was the production of creatin and creatinin in the blood and urine. For example, the normal quantity of creatinin in urine is given by some authorities as ranging from zero to 80 mgs. per 100 cc. of urine. In a series of thirty-three approximately successive patients it was found to vary from 40 to 260; and when we study the patients we find one, for example, with 200 mgs. was ill in our ward with a very bad heart involvement, which rapidly cleared up after the removal of her dental infections. Another, 240, had a near nervous breakdown. Studies that have been made of various expressions of acidosis have demonstrated the increase in creatinin with the acidosis.

Noel Paton[23] has shown that creatin may be regarded as a substituted guanidin; and Watanabe[24] has shown that the injection of guanidin directly into rabbits produces an acidosis with development of albuminuria and casts. I have, accordingly, undertaken to establish somewhat of the relationship between the toxic substance produced in infected teeth and guanidin. One of the methods of approach has been to defibrinate freshly drawn rabbits' blood and to add to one tube of it 200 mgs. of a 5 per cent solution of guanidin carbonate to 2 cc. of blood. A second tube was similar except the use of guanidin hydrochloride instead of the carbonate. In a third tube of the blood, pieces of a crushed infected tooth were placed and a fourth tube was used as control. The control tube showed an alkalinity index of 40.6.

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[23] See bibliography.

[24] See bibliography.

The tube with the guanidin carbonate showed an alkalinity index of 51.4, the guanidin hydrochloride 24.2, and the blood with the pieces of crushed tooth 68.2. It will be noted that, whereas the ionic calcium of the normal blood was 11.1, when the crushed tooth was placed in it, its ionic calcium decreased to 8.2. Since the quantity of alkali which was introduced with a small piece of tooth was so insignificantly small that it could not possibly account for, from a chemical standpoint, the marked increase in base in the blood, from whence and how did it attain that state, for the change in the capacity of the blood plasma to absorb 40.6 grams of carbonic acid per 100 cc., increased to 68? This immediately suggested that the reservoir of the blood had possibly been drawn upon.

In Chapter 43 I have briefly reviewed the process of development of incompletely oxidized products which are acid in reaction and which must be immediately neutralized, for which purpose the body uses its most available bases, and in the absence of others seems to use the calcium. Henderson and Spiro have shown that the alkali of the blood is largely carried in the red blood cells though there is a sufficiency for the needs of the blood plasma, as bicarbonate, in it. The red blood cells are capable of taking up acid as carbonic acid increases in the body, and carry it to the lungs where it escapes as carbonic acid. The mechanism which controls this equilibrium, while probably purely a physico-chemical one, is one of the most delicate and exact of all the processes of the body. May it not be that the toxin contained in an infected tooth, which is capable in ten minutes' time so to change a few cubic centimeters of blood as to reduce the ionic calcium 10 to 50 per cent, even though the root tips only of the whole tooth are placed in the blood, with therefore no appreciable loss in weight of the tooth itself, may be able to produce these far-reaching changes in both ionic calcium and hydrogen ion concentration either by entering into combination with some of the hormone or enzyme substances or by acting as such itself?

When we review some of the outstanding effects of dental infections, we find among them a tendency of the individuals suffering from them to be underweight except in those cases of tissue infiltration with edema, where their appearance may be very deceiving. I have also shown that the placing of the filtered washings from teeth into rabbits, tends very markedly to reduce their weight, and, perhaps, most important, starts a series of metabolic changes which go on to complete emaciation and death even though the evidence strongly indicates no living organisms were introduced. Indeed, this process has been produced with heated tooth extracts and with heated infected teeth and even with some autoclaved teeth. We seem, therefore, to be dealing with a substance which may or may not have properties in common with guanidin, which matter our studies are endeavoring to disclose, but which toxin acts directly upon the fundamental controlling mechanisms of the body. It we will think of the smallness of the quantity of insulin, one four-thousandth of a gram, which, when injected into a rabbit, will so activate the mechanisms of the body for burning up sugar as to reduce the blood sugar so rapidly and completely as to cause the death of the animal, and when we realize that without any insulin, the rabbit or human is entirely unable to metabolize sugar, we realize what infinitely small amounts of the activating substances will be required for life's processes. Let us think for a moment of the thyroid. Marine has shown that a couple of drops of iodin placed on a dog's tongue at the time of the development of a goiter, will prevent the typical development of the pathological process, and also that the administration of a few grains of potassium or sodium iodide, or iodin in any suitable form, to growing girls once or twice a year will completely protect them from the development of goiter, and that animals so suffering can be cured by these almost incalculably small quantities in proportion to their body weight. Or again when we think of the quantity of Vitamin B that is necessary for an animal to prevent the development of the typical lesions of the nervous system, we find it to be the infinitely minute quantity of one two-hundred-thousandth part of a gram per day per kilogram of weight. Or again, when we think of the quantity of toxic substance which extracted from a tooth will be sufficient to produce marasmus in a rabbit, we find it to be only a minute fraction of a milligram. We have not been able to measure it, it is so small. We are, therefore, dealing with a substance in these infected teeth which, like the activators of metabolism and the hormones controlling function, have to be dealt with and considered in terms of their effects rather than in terms of their mass. When we reflect the popular opinion regarding the quantity of dental infection necessary to produce disturbances and compare it with the facts, we find an ample explanation for the divergence of opinion.

But there is another phase of this problem which must be considered in this connection, and that is the clinical in its relation to the removal of dental infection, for if dental toxins and dental infections have so far-reaching effects on metabolism and catabolism, we should get many important data from the study of the individuals from whom these infections have been removed. This very important phase of this problem has not been neglected, but is so voluminous as to require a separate volume approximately the size of this one, and since the data have been simultaneously developed, it is being simultaneously published. It is important, however, to state in connection with the argument of this chapter that the removal of dental infections from not a few hundred but from several thousand individuals (many of whom have had chemical and morphological studies of the blood and fluids of the body as controls for the symptomatic change) has developed a fund of information which clearly establishes that the removal of the dental infections has completely changed the symptomatology, to accomplish which, fundamental changes were produced in the metabolism and catabolism of their bodies.

If lack of space did not prevent, we could, by briefly reviewing the clinical researches that are reported in Volume Two, present many illustrations of the change of metabolic processes by the removal of dental infections, and these would relate to a great many, if not nearly all, of the important organs of the body. I will illustrate with just one case which is reported in detail in Chapter 66 on Eyes. The woman presented with marked exophthalmic goiter. Exophthalmos is a symptom that is so clearly related to the functioning of the thyroid that we can without question classify it as a controlling factor in metabolism. There are two phases of the case to be noted here especially. The first is (and we have many cases illustrating this) that there was marked improvement in the appearance and condition of her eyes in a very few days after the removal of her dental infections, and in the chapter referred to it will be seen that her protruding eyes reduced to practically normal position and size in a few weeks' time. The other important item to note is (and this is also illustrated with the photographs of the rabbits in that chapter) that several rabbits that were inoculated intravenously with the culture from her infected teeth when they were removed, developed within forty-eight hours very marked bulging exophthalmos, a condition that has not developed in 1 per cent of 1200 rabbits inoculated with miscellaneous cultures. This seems strongly to suggest that her dental infection was directly affecting her metabolism through its effect on the thyroid, as was also evidenced by the very great improvement of her nervous and heart symptoms.

Similarly, we might review disturbances of hearts, kidneys, gall-bladder, ovaries, testicles, nervous system, digestive system, special tissues, etc., and cite case after case as part of the experimental data of this chapter. I will, accordingly, ask the readers of the second volume to keep this phase in mind—namely, the relation of the dental infection to those forces which control metabolism and catabolism.

I would, therefore, summarize as follows:

Since dental infection affects directly the ionic calcium of the blood and the acid-base balance of the blood, it is affecting two of the most fundamental factors in all of life's processes, which, if continued, will of necessity produce degenerative changes in the tissue so altered, for no change can express itself in function without a physical or physicochemical change in functioning tissue. Henderson has stated that of all the regulating mechanisms of the body, the acid-base balance is the most important and far-reaching. This is so because every process of body function is dependent directly upon hydrogen and hydroxyl ion concentration. If, then, the toxin of dental infection can influence Nature's most fundamental governing process, we find an important new light on the etiology of the degenerative diseases, and in the second volume, which is a continuation of this study from the clinical pathological standpoint, I have undertaken to interpret in the terms of the individual cases, the various processes concerned in so far as our present knowledge makes that possible. When we reflect that the various expressions of shock are primarily due to acidosis, as shown by Crile, Cannon, Wright, and others, and further that all symptoms of an acute shock may be produced in experimental animals by the introduction within their bodies of the small amount of infection and toxin in an infected tooth, and further that humans carrying dental infections for a long period develop a state which might be expressed as a low-grade and chronic shock, we get a new meaning for this type of toxic invasion. I would, therefore, present the foregoing as simply a preliminary report and stress the necessity for more exhaustive researches on these fundamental problems.

I have endeavored to make the reports of these studies as brief as possible in order that this volume might not be too cumbersome. It has already more than doubled the dimension originally intended, which has compelled the publishing of this report in two volumes instead of one, and notwithstanding this brevity I have presented only a small fraction of the data which I have accumulated in these various studies. The presentation of a new basis of interpretation, which I shall give in the succeeding chapters of this volume, together with my interpretations of the clinical pathology, as presented in the next volume, constitute this first preliminary report. I have, however, in course of preparation, data on the practical application of these various processes with a desire to assist the members of the dental and medical professions in dental diagnosis, prognosis, and treatment, and, primarily, in the prevention of the dental lesions. Of necessity this work requires a great deal of time and the expenditure of an almost unbelievable amount of energy and, incidentally, a very large expense. The importance of the work makes all these justified, subject always to the uncontrollable limitations of resources and physical endurance. In other words, it will take many months of additional work to complete Volume Three on Dental Infections, Their Diagnosis, Prognosis, and Treatment.

SUMMARY AND CONCLUSIONS.

I will, therefore, briefly express the conclusions of this chapter as follows:

> **Dental infections disturb directly the acid-base balance of the blood and thereby prevent the catabolic processes which would remove from the body the products of tissue reaction, food intake, etc., as inert end products, (chiefly as urea, carbonic acid, and water). This disturbed catabolism directly and in association with other disturbing factors, results in the production within the body of acid products which are neutralized by the body with difficulty and at the expense of other vital processes. Their retention within the body injures not only the tissues involved normally in the process of their elimination, but disturbs directly the processes of metabolism and catabolism. These express themselves as disfunctions, and organ and tissue degenerations, and constitute an important factor in the morbidity and mortality of even our most advanced civilizations.**

Since the hydrogen and hydroxyl ions constitute by their mutual relationships and proportions not only the mechanism of control of the acid-base factors, but by their proportion in various fluids determine the functioning qualities of various organ and tissue cells, they probably constitute the most important hormone of the body, and any forces which disturb their relation will thereby disturb the functioning of practically every cell of the body of the individual, which processes, if continued, result in structural change and disfunction and organ degeneration. Since dental infections exert so direct an influence on this fundamental hormone, they become directly the cause of extensive and destructive degenerative organ changes.

See bibliography references 38, 39, 40, 41, and 42.

CHAPTER XLV.

INTERPRETATIONS.

THE LOCAL PHENOMENA OF DENTAL FOCAL INFECTION.

DISCUSSION.

Focal infection, whether dental or otherwise, resolves itself fundamentally into a warfare between two biological units, one unicellular and the other multicellular, the former a parasite on the latter. Under ordinary conditions the invader is dependent upon a defect in the cellular structure of the latter, which defect may take the form of traumatized and therefore abnormally nourished and injured tissue, or of partially poisoned tissue, the result of toxic invasion or other foreign poison. The invaded host is thereby handicapped in its warfare against the invading parasite. True, there are a great many different types of invading organisms, some generating a poison which paralyzes or kills the tissue in advance of the invading organisms, and thereby prepares the way for them. Still others live in the tissue without apparent local irritation to that tissue. They may generate exo- or endo-toxins and they may select any of the varied tissues of the body as their habitat, some even limiting their activities to the cells of the blood.

The disturbances with which we are concerned, whether of the teeth or of other tissues, but particularly the former, which produce local foci that develop toxic substances and bacteria which invade the body, are dependent pretty largely upon an organism or group of organisms having quite definite local and systemic characteristics, both from the point of their morphology and of the reactions they produce. For convenience we speak of the lesions they produce as the rheumatic group lesions, rheumatism being but one of the many disturbances. We are particularly concerned with the characteristics of the invading organism in this type of lesion, since so many of the deficiency diseases (old age diseases) are indirectly or directly influenced, and in many instances caused, by these local processes.

This entire group of researches is primarily a study of this warfare in its various phases. Since it is a contest between two biological units, our first problem seems clearly to establish the responsibility of each. Arguing from analogy, we saw in Chapter 2 that if we will consider this invading organism as having similar characteristics to those of the many infectious diseases with which we are so familiar, and which have been so far-reaching in their devastations, we will expect of it, when in this type of lesion, that it shall have brought into its environment the weapons which prepare it for the particular type of expression which it will later develop. If we will think of any of the biological units which we are associated with, we find that they have very limited capacity for adaptation. The beaver must have soft wood trees to gnaw and live upon, and water in which to swim. The feline kind must have animal life to live upon; and, similarly, we find species which will limit their activities to very narrow ranges throughout the entire field of life.

It is, therefore, natural that we should have expected that the organisms with which we are concerned in this special study, would have very definitely fixed qualities which would determine their elections and expressions. We found, however, in Chapter 2 that contrary to this natural expectation, which is almost universal in its acceptance, the organisms with which we are concerned in this type of pathological process do not bring with them their essential characteristics which perforce establish and predelect the characteristics of the local and systemic expression. On the contrary, the different morphological characteristics and classifications of the varieties are found in the different types of pathological expression in the order of chance, with utter disregard to the biological differentiations. We further found that while this type of lesion is produced almost entirely by a group of organisms, which we speak of as streptococci and diplococci, growing in one or the other form, and largely in accordance with the media in which they are growing, they have the remarkable property and capacity which enable them to adapt themselves to most extreme and unexpected conditions, even coming to grow luxuriantly in concentrations of poison, which completely inhibited their growth and devitalized the earlier generations which formed a part of their antecedents, before they had availed themselves of this wonderful quality of adaptation; and further we found that these non-spore-forming organisms have the capacity for taking on forms which are very similar to the spore formations, in effect, of the truly spore-forming varieties of bacterial cells.

We have, therefore, as the first important goal in the analysis of this struggle between these two biological units, that the invading organism, while infinitely the smaller, is destined to win the battle if only time enough may be granted, largely on the basis of this one quality of its marvelous ability for adaptation to its environment. We have in this wonderful quality, however, perhaps one of the greatest forces in the development of our animated life. It has been by this quality of adaptation, that those earliest unicellular forms developed into the more resistant and more adaptable multicellular forms and all the way up, for some of the writhing monsters in the warm pools where the waters dried up into mud developed their fins into legs and their gills into lungs, etc. This law of adaptation enabled these creatures through long ages of time to go out upon the hardening slime and adapt themselves to a changed environment; and, ultimately, by adaptation, the forms of life adapted to all the conditions from the torrid to the frigid zones; and even so man has grown, for archeologists show us that man made his greatest advancement out of the stone age into more efficient methods of living, partly as a result of the hardships of the ice age.

When we review results of the many hundreds of rabbit inoculations with cultures grown from infected teeth, it is a matter of profound importance and significance that almost universally all other strains are killed off in the animal's body except the diplo- and strepto-coccal forms. It is true that in a few instances staphylococci will also be isolated, but, proportionately, these cases are rare; and aside from these two, it is an exceedingly rare exception to find any other oral type of infection. In later chapters, for example, I record some spirochete systemic involvements. In our studies in Chapter 41, we found that when the lymph extracted from humans and from rabbits was inoculated with the mixed strains and varieties that grow in the human mouth, the principal strains to grow out were the diplococci, streptococci, and staphylococci. This brings us to ask why these are the facts. May it not be, and, indeed, is it not probable that again the law of adaptation has been at work, that as these organisms have grown as commensals in the mouths of all humans during the tens of thousands of years of their existence, they have come in contact with the body fluids through gingival abrasions and carious teeth until they have actually come to live in and upon modified normal tissue fluids? But the question may be asked, "Why is this not just as true of all the spirochete and bacillary forms?" The answer to this may be that the local and systemic defense, or rather disturbed defense, produces an environment which, because of hydrogen ion concentration changes and other biological and chemical factors, these latter do not find within the range of their adaptability; nor, indeed, do we find evidence that they have nearly so great a capacity for adaptation as the diplostreptococcal and staphylococcal varieties.

We would, therefore, summarize the Local Phenomena of Dental Focal Infection as a warfare between two biological units, one unicellular with a most remarkable capacity for adaptation, the other, the host, multicellular, with normally in normal tissue a defensive capacity adequate to combat and obstruct the invasion of the former. When the defense of the host breaks at any point, the invader through its marvelous capacity for adaptation increases its attacking power and develops its defensive factors to resist the attacking mechanisms of the host. The fundamental point of break, therefore, is in the failing defense of the host, and our problem largely consists in studying the various changes of environment that may be provided by the host.

CHAPTER XLVI.

INTERPRETATIONS.

THE PHENOMENA OF LOCAL REACTION.

DISCUSSION.

In the preceding chapters we have reviewed several researches which were undertaken to verify or correct the generally accepted premises on which our interpretations are made. These studies have shown very clearly that things are not always as they seem to be. Whereas we have looked upon the changes that have occurred about teeth, as being directly both the result and the measure, in general, of the infection process, we found, contrary to the accepted interpretations and expectations, that the structural changes do not denote either the quantity or quality of the infection in a sense that we have understood.

In Chapter 1, we found that there are very definite limitations to the capabilities of the Roentgen-rays in the matter of disclosing either the presence or extent of dental infections.

In Chapter 2, we found that the organisms involved in various dental infections may have any of the several biological characteristics of the various groups of streptococci, irrespective of either the type of local expression in the affected tooth or the systemic involvements of the patient.

In Chapter 4, we found by an analysis of many hundreds of individuals that they do not have comparable histories and also that they do not have comparable expressions of similar dental infections; that they do tend, however, to divide into groups, the members of which groups are so similar as to be directly comparable.

In Chapter 3, we found that a given dental infection may express itself in a large variety of local ways in the local tissues about the tooth, and that all these variations depend upon conditions which are inherent to the patient.

In Chapter 5, we found that there is a very direct relationship between the type of the local expression of the dental infection and the systemic reactions.

In Chapter 6, we found that absorption might be caused by other irritants than dental infections.

In Chapters 7 and 8, we found that in both dental caries and periodontoclasia there is a very definite tendency of pulps to become infected and undergo degeneration changes with the approach of infection from these sources.

In Chapter 9, we found that people with a tendency to rheumatic group susceptibility have also a marked susceptibility to dental caries.

In Chapter 10, we found that the gingival infections do not tend readily to develop about the teeth of people with marked susceptibility to rheumatic group lesions, and their active process is more frequently found in individuals at a time when they have not a susceptibility to rheumatic group lesions.

In Chapter 11, we found a marked relationship between the tendency to gingival infections and a tendency to extensive periapical absorption with a given dental infection.

In Chapter 12, we found that the extent of the absorption not only is not a measure of the danger but frequently is an accompaniment of complete absence of rheumatic group lesions.

These data have revealed a progressive type of rarefaction with an increase of systemic defense, in contradiction to the accepted theorum that the extent of infection is a quantitative measure of the infection and hence of the danger (or the extent of systemic involvement). This seems like a paradox, and it is not strange that frequently when we have expressed this new interpretation, that the first reaction has been not to accept it. Incidentally, this was our own reaction for a long time.

Let us study the nature of the forces operating about the root end of an infected tooth whose pulp is already putrescent. This degenerating pulp consists of the products of bacterial activity including the bacterial toxins, tissue degeneration products, living and dead organisms, and mechanical interferences such as pressure of fluids and presence of gases. A first result of all irritation is stimulation. The extent and nature of this irritation determines the extent and nature of the inflammatory reaction. There will be an engorgement of defensive factors in the surrounding tissues, the marshalling of which requires marked dilatation of the blood vessels to take care of the additional blood for the defensive and offensive operations. This constitutes the first stage of inflammation. With the marshalling of lymphocytes, bacteriolysins, antitoxins to neutralized toxins, etc., there will be a marked liberation of antagonizing substances and their products into the field of no man's land at the point of most intense battle between the invading organisms and the defending tissues, which is directly the result of the warfare, for Nature is trying to establish a quarantine. If she succeed, it will only be because she maintains that active warfare. But such a warfare means a constant accumulation of the products of the warfare, phagocyted leucocytes, neutralized toxins, all taken care of by Nature's mechanism or irrigation to eliminate pollution. Which will require the larger refuse disposal irrigation system, a very mild local reaction or a very severe one? There is no question as to which will. Our roentgenogram records some characteristics of the battlefield, whether it be large or small, or whether a truce be on, or whether, as it may be, no adequate quarantine has been established.

A study of individual cell reactions shows that the difference between an active reaction in one direction or its complete reversal is dependent upon the amount of stimulation of the cell. For example, the same cells that lay down some calcifying structures will proceed immediately to take them up again if pressure is applied to them, and this reversal process may go on as long as those tissues live. Similarly, tissues may be made to lay down bone or take it up again with other forms of irritant, as, for example, retention of heat, prevention of radiation, chemical vapors, contra-irritants, etc., etc.

But we have said that, in general, the organisms are not different in different cases, or at least that the effects produced are not the result of difference in definite strains of organisms. What, then, is the force that determines whether or not this given irritant, the bacterium involved, (which as we have implied or said we believe to be quite similar in the various cases except that it is made different by its environment) will produce a large or small chamber in the bone about the root apex? We have only to think of the wide range of effects that will be produced on various individuals by the same irritants. For example, mosquito bites have almost no effect on some people, while on others they not only produce violent local inflammations with swelling and great pain but such violent toxic effects on the whole system as to make the individual positively ill. The difference is not in the irritant in this case; it is in the reaction to the irritant, which factor is primarily, an activity of the host called forth in response to the invading irritant. Until we have had typhoid, we have little or no attacking power against the organism of typhoid when it gets into our blood stream. When we have had that infection in our system for a sufficient number of days, we have built up a mechanism of attack; and the difference between an individual with that defensive mechanism which constitutes his immunity more or less perfect ever thereafter, and the individual who has no immunity and becomes readily a culture ground for the organism, is precisely that power to react.

Let us think now of the phenomena of local reaction to dental infection in terms of reaction rather than in terms of attacking power of the invading bacterium, and apply this interpretation to the various experimental problems as we have been reviewing them. Returning again to the problem of Chapter 4, Systemic Structural Changes, we found that human beings divide themselves into groups, the members of which groups are comparable to each other, while the members of the different groups are not comparable; and the fundamental differences between these individuals on this basis are those qualities which make them competent to react against rheumatic group infections. Those with an absent susceptibility have so good a defense that they do not develop rheumatic group lesions. Their local dental infections are invariably accompanied by extensive areas of rarefaction; in other words, an efficient and adequate local reaction. The second group, those with an acquired susceptibility, have had that high defense, until by overload it has been temporarily broken. In this state of acquired susceptibility their local reactions about their dental infections are very poor. In the third group, those with an inherited susceptibility, we find that in the progressive groups, from mild inheritance to very strong, there is a progressive lack of ability for defense against the invading organisms with a consequent progressive development of lesions as the local reactions become less and less acute. In other words, as the defensive reaction diminishes at the point of invasion—namely, the infected tooth—the systemic susceptibility increases, whether acquired or inherited, except that the prognosis is very different in the individual whose defense is normally high from that of the individual in whom it is normally (by inheritance) very low; and similarly, we might apply this new viewpoint to all the different phases of the problem as expressed in this series of researches.

Let us apply this interpretation to the gingival infections. Figure 262 shows a typical and extreme case. Seldom do any of us ever see a mouth with so much free pus exuding from around the teeth. The bicuspids and incisors are so literally floating in pus that with every movement it exudes in all directions. Note the

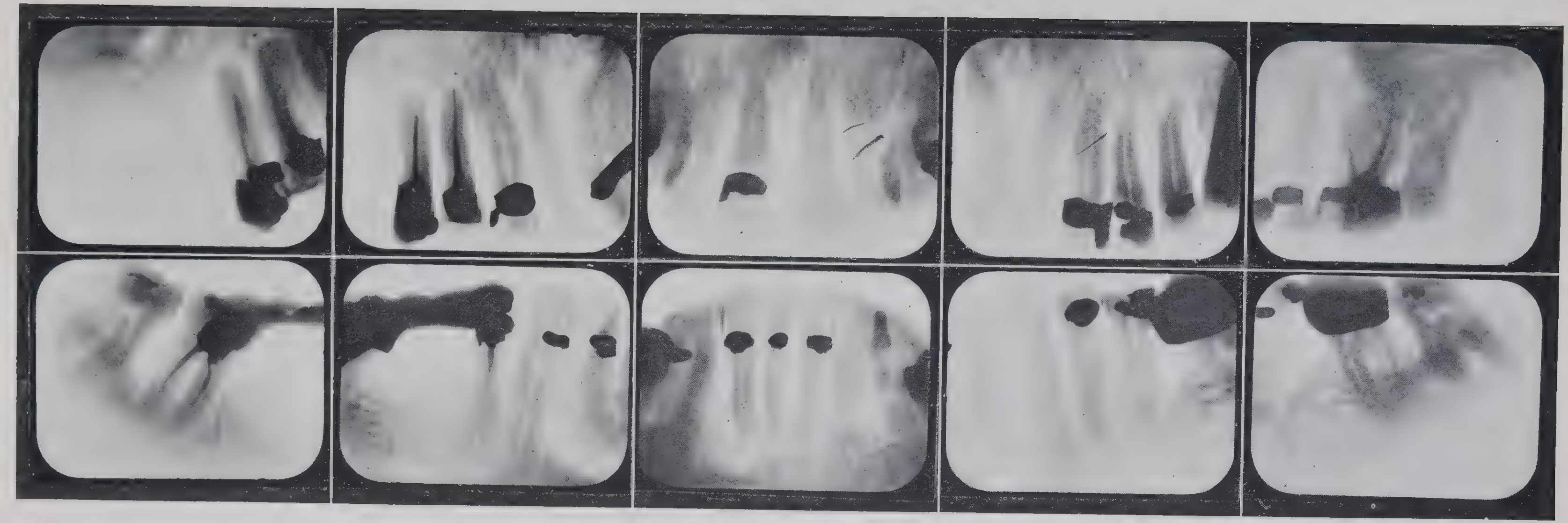

Figure 262. Case No. 1268. Roentgenographic appearance of a case with a profuse flow of pus, exuding with every movement of the teeth. Neither the patient nor any member of the family group had had rheumatic group lesions. Chemical analysis of blood and urine reveals that he has already a severe hyperglycemia and glycosuria. The patient had no suspicion that he had diabetes.

very extensive alveolar absorptions. Surely, if any person would be sick, if a quantity of pus could make him so, this man would be. But what are the facts? He is forty-six years of age, has never had a moment's rheumatism or neuritis, or any other affection of which he knows; nor have any of the members of his family, either on the father's side or the mother's side, or brothers and sisters. His mouth has had wretched care; deposits are everywhere; there has been no worthy effort at prophylaxis. Why has he not broken? Because he has established an adequate quarantine, though at a terrific cost, for the battle-ground has extended until it has involved tissues nearly to the apices of many of the teeth and quite to that point on several. What is his classification? Up to the present—absent susceptibility. How long will it be so? Impossible to tell but probably not long, for already his urine shows 4.46 per cent of sugar, and his blood 295 mgs. of sugar per 100 cc. (Normal threshold of danger about 120. Normal blood sugar 70 to 100.) The ionic calcium of his blood is 12.32 mgs. per 100 cc., one and one-half above normal. His mother had diabetes. How long will the quarantine be kept up? Until his defense goes down with Flu, dental infections, overwork, great grief, or any of the many complications and contributing factors. Then what will happen? When the quarantine is withdrawn from all this area of attacking enemy, it will rush in and overwhelm his system; and this type of man often goes down like an avalanche with diabetes, nervous breakdown, Bright's disease, etc. This man's impending danger is already upon him as an unsuspected diabetes, though he thinks he is well, for the islets of Langerhans of his pancreas are probably already diseased either from the dental infection or other sources. He may be helped by the administration of their extract, insulin, or the pancreas injury or disfunction may be related to other causative factors than the dental infection. These are discussed in the chapter on Diabetes. What will the prognosis be? If the source of infection is removed and his defenses thereby restored, he will tend readily to come back to his normal, which is high, provided that the functioning of some fundamental tissue or organ has not been permanently impaired. But just here is his great danger. What will be the expression of his periodontoclasia when he has lost his defense? Much less pus formation because there is much less local warfare. Indeed, it will become the camping ground of a new type of organisms. Streptococci and staphylococci, chiefly the former, will take up their abode in the necrotic hard and soft tissues. Fusiform and spirochetes will largely disappear with the reduction of the alkalinity of the exudate poured into the gingival pockets and the cutting off of special nutrient materials on which they depend. Where will the new invaders, the streptococci and staphylococci, go while that defense is broken? They will have a pass practically to every part of the body, for that is what constitutes the absence of reaction.

There are many phases of this problem upon which important researches must be conducted. In the chapter on Ionic Calcium of the Blood in Relation to Focal Infections and Systemic Defense, and as demonstrated in the many clinical histories in the succeeding chapters in Part Two, we see that there is an optimum ionic calcium of the blood below which there is a tendency to the rheumatic group lesions, and above which there is a tendency to periodontoclasia, diabetes, acidosis, osteomalacia, etc. The former tends to be associated with condensing processes in association with rarefactions. Carbohydrate metabolism, alkalosis, alkalipenia, acidosis are all related factors and they thereby become direct means for checking the defensive factors and pathological tendencies of the individual.*

In our introduction we referred to the fact that internists and dental practitioners have been saying, "How can it be true that dental infections are such important etiological factors in rheumatic group affections when so many individuals have such large quantities of infection present in their mouths, and yet have none of these disturbances?" This new interpretation seems to explain for the first time this paradox, for the thing they were seeing was the surest kind of proof of this type of reaction of which we are speaking; and the cases in which the reaction was absent were interpreted not to have any occasion for reaction, as will be abundantly demonstrated in our clinical cases. The individuals with the acute rheumatic group lesions are, in the great majority of cases, those with no more cause than this group we have just been discussing, but they are individuals who are not maintaining the adequate local quarantine about their teeth.

But, as we have seen, we are not dependent upon the indirect evidence to establish that this is fundamentally a warfare between an invading organism with its mechanisms of attack and defense on one side, and the host with its defensive mechanisms and devices of attack on the other, which latter are established and maintained by the host as a permanent system of quarantine so long as the dental infection exists. In addition to the indirect or clinical data, to which we have referred, we have seen in Chapter 38, The Nature and Function of the Dental Granuloma, and Chapter 41, Variations in the Defensive Factors of the Blood, that both the granulomatous tissue, when in good functioning condition, and the normal blood structures, particularly the leucocytes, furnish substances which not only have the capacity for inhibiting the growth of the organisms, but actually devitalize and literally digest them. It is not an accident or a mere coincidence, but a fundamentally associated fact, that the individuals with that type of blood and with that type of granuloma are those without clinical histories of rheumatic group involvements, and this notwithstanding the abundant evidence in their cases of an ample infection in the involved teeth. Our problem, then, simplifies itself to a study of the relative and actual efficiency of the local and systemic mechanisms in conjunction with the presence and absence of dental infection; and a very small quantity of infection, existing without the presence of the defense, may do the individual much greater harm than will a very much more extensive infection in the presence of these mechanisms of defense.

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*Notwithstanding the above general principal, some types of arthritis are locally characterized by degenerative processes and systemically accompany abnormally high ionic calcium of the blood.

SUMMARY.

We would briefly express our interpretation of the Phenomena of Local Reaction as follows:

> **The structural changes which develop about infected teeth are expressions, primarily, of the type of reaction of the host to this irritant and, as such, are therefore, when understood, a direct means for interpreting that individual's defensive mechanism.**

CHAPTER XLVII.

INTERPRETATIONS.

THE PHENOMENA OF SYSTEMIC EXPRESSIONS OF DENTAL INFECTIONS.

DISCUSSION.

The researches which we have reviewed in the preceding chapters have many of them been carried out to ascertain further fundamental data regarding the relationships between systemic expressions and focal infections, with particular reference to dental focal infections. In Chapter 4, which is a review of a study of the factors which individuals have in common with regard to susceptibility to, or immunity from, systemic involvements of the rheumatic group type, these indicated that this quality is persistently present in certain individuals and persistently absent n others, while in still others it is a variable quality appearing only under severe stress and overload, and that these qualities of susceptibility and immunity are not related to the particular type or strain of organism present (Chapter 2) or to the particular type of lesion. It is also demonstrated that this quality is very closely associated with the forces which control in the processes of heredity. For example, there were more cases of heart involvement in one hundred of seven hundred families than in the other six hundred.

In Chapter 5, in studying the relationships between local and systemic infection, we recorded the following conclusion: That a given infection may express itself by causing an absorption, even extensive absorption, or may produce very little absorption. or none at all, of bone tissue, and may even produce condensation of the bone, *all depending upon inherent conditions of the patient or host.*

In Chapter 9, we found that there was a marked relationship between the predominance of caries and the susceptibility to systemic disturbance.

In Chapter 10, we found that susceptibility to systemic involvement was not in proportion to susceptibility to periodontoclasial infection.

In Chapter 11, we found that there was a direct relationship between the tendency to gingival rarefaction and bone absorption and extensive periapical rarefaction and absorption accompanying periapical infection.

In Chapter 12, we found that the relation of the extent of the absorption to the danger was, in general, in inverse proportion to the latter for a given infection.

In Chapter 13, we found that the discharge from a fistula from a chronic periapical abscess, is made up almost entirely of neutralized products, leucocytes and phagocyted organisms.

In Chapter 16, we found that comfort and serviceableness were not necessarily dependable criteria or evidence to be depended upon as symptoms.

In Chapter 21, we found that, whereas the normal body has what may be normal as a defense for that patient, that standard may be greatly lowered by various types of overload, such as acute infections, grief, pain, hunger, focal infections, etc.

In Chapter 22, we found that the quality of elective localization on the part of bacteria is a relatively transient quality which since it is easily lost by placing in a changed environment such as an artificial culture medium, rapidly disappears and, in general, seems to be directly related to the environment furnished by the circulating forces of the patient's body rather than the local dental conditions.

In Chapter 24, we found that this quality of tissue affinity or elective localization is one which relates largely to the particular organ or tissue rather than to the entire system, with, however, systemic factors, one of which is calcium metabolism.

The similarity of these studies reveals that the quality of susceptibility or immunity to systemic involvements is not determined by qualities and conditions which obtain in the focus of infection, but have to do with various tissue defensive factors together with the general defensive factors of the body; and that while the local conditions are not the primary factor in the systemic susceptibility, there are distinct characteristics of the local expressions of the focal infection in both the condition of marked systemic susceptibility and the condition of marked systemic immunity; and, further, that these systemic qualities, which constitute that susceptibility, have to do with the ancestry and progeny; also that these qualities relate to individual organs and tissues of the body in such an orderly manner that we can see distinct evidence of true mendelian factors. In addition to these inherited susceptibilities, tissues are greatly influenced by overload changes, among which are those which disturb nutrition and metabolism. These may be divided into groups: Infections such as influenza which suddenly and very definitely destroy the normal defense to streptococcal infections, so much so that one of our high authorities has suggested that when the people living in our civilized communities of today die, in the great majority, the final blow will be struck by an organism they are carrying within their bodies, and for which they have, under ordinary conditions an ample defense. I found, as I have shown in Chapter 21, in my analysis of conditions in hospitals in the Flu epidemics that the incidence of systemic complications with, and following the Flu, was about two and one-half times greater among patients with extensive dental infections than in those without dental infections. Next to influenza we would be inclined to put pregnancy as a condition of overload which predisposes to rheumatic group disturbances. Fear, grief, worry, focal infection, etc., are all very direct influences in reducing normal defense.

A very important contributing factor to a condition of susceptibility is found in disturbed nutrition; by which we do not mean people who are not in position, by sheer poverty and uncontrollable circumstances, to get food, but we will include vast numbers who are starving their normal defenses by improper eating. Another and very important factor has to do with the nature of the focus of infection; whether its contents are under pressure, whether the quantity tends to overwhelm the available defensive factors, or whether they had tended by long duration to exhaust the defensive effort. It is said of the Eskimos on certain northern islands, that every Eskimo who was exposed to measles died; yet, for centuries, no Eskimos died from measles because no Eskimos were exposed to measles on said islands.

It seems in large measure true, exceptions to which I will discuss elsewhere, that individuals with marked susceptibility to rheumatic group lesions may for long periods, as are the Eskimos, not be affected because of complete absence of exposure to streptococcal proliferation within their systems; and, herein, lies our great danger. A dental infection is safely and permanently protected even within Nature's fortress. Indeed, it develops and supplies the organisms from within an armored blockhouse into which none of the defensive factors of the host can successfully enter to exterminate them, yet into which that host furnishes a continual supply of pabulum and food in the circulating plasmas brought to that tooth. Under what conditions will the defense be high enough? Just so long as every organ and tissue of that body can safely defend itself against the circulating poisons sent out into the system from that fortress for creating diabolical poisons, provided that the larger proportion of the toxic products and invading organisms may be destroyed as they leave that fortress.

We find ourselves, then, face to face with the same problem which we had in the preceding chapter, the problem of effective local reaction about the tooth. If the local reaction is adequate, it will, incidentally, as we saw in the last chapter, produce extensive rarefaction as part of the process of warfare. It will primarily preserve the rest of the body from exposure by the maintenance of that efficient local quarantine. When that quarantine breaks down, that tissue which is most susceptible because of inheritance, with or without an additional overload, will be the one that will break If all tissues have normally a very high defense, the break will, in all probability, come in the nervous system. When will it come? That depends. When the overloads and normal body defenses together have reduced the balance, so the pendulum swings in favor of the attacking organisms. It may not be until ninety years of age; it may be at sixty; or it may be at thirty; but it *will* be, sometime, for it is a fight to a finish with every one of us and, ultimately, we lose. But both our clinical data and our experimental research demonstrate that, only that individual will reach the eighty or the ninety mark and carry his dental infections, who also carries until that time a well vascularized special tissue which Nature will build about the source of exit of his dental infection into his system. Whether we call it a granuloma or otherwise, when it becomes a degenerating, inefficient, defensive membrane, the warfare is not completed at the first line trench, and some organ or tissue will break.

CHAPTER XLVIII.

INTERPRETATIONS.

THE PHENOMENA OF RELATIONSHIPS BETWEEN LOCAL AND SYSTEMIC EXPRESSIONS.

DISCUSSION.

In the three preceding chapters we have discussed and suggested interpretations for the various data presented by the researches on dental infections from the standpoint of the phenomena of bacterial invasion, local reaction, and the phenomena of systemic expression, and found that underlying each were certain consistent and quite regularly observed expressions which are sufficiently constant to be looked upon as being the result of definite laws of cause and effect. In this chapter we desire to study the two latter groups of phenomena with a view to observing whether in some particulars they may be related each to the other, or both to the same cause. In general, these researches have disclosed that the quality, which we recognize as an ample systemic defense, is found in an individual who, when he or she has a dental infection at a root apex, tends to have an extensive reaction with an accompanying rarefying osteitis. We will, in this chapter, use this term as indicating that local condition, whether at a root apex or accompanying an irritation at a gingival margin, for these studies have shown that these individuals with high defense show this same marked tendency to absorption of bone as a result of irritation, regardless of its location, and that these individuals readily develop the clinical condition which we have come to look upon as periodontoclasia, or pyorrhea alveolaris; and, conversely, we have seen that individuals with a low systemic defense to streptococcal infection, tending to express itself systemically as some of the rheumatic group lesions, have local dental infections which tend to express themselves as an absence of extensive rarefying osteitis, or with a definite condensing osteitis, and in whom gingival alveolar absorption is almost completely wanting; in other words, very little periodontoclasia, or pyorrhea alveolaris.

Are not these two conditions of local type of expression and systemic susceptibility or immunity, symptoms of a common condition or effects of a common cause? To approach this complex question let us look at some of the serological data to see if with even our present meager knowledge of blood, saliva, and urine chemistry, there are any items that will throw light upon this problem. If we will take a patient whose general history has shown that his general condition has been one of an absence of involvement, but who has, because of acquired conditions, developed that state which we speak of as susceptibility to some type of rheumatic group lesion, we should, by a careful analysis of the various sera of the body, get information that would at least be suggestive, though it will only be by a large number of studies that we will be justified in making conclusions.

The variations from normal in various factors which may be found within the body during life, may have a wide or narrow limit of change, dependent upon the nature of that factor, both in health and disease. For example, there may be a relatively wide range of variation in body weight in food ingested, liquid ingested, excreted, and radiated, or even carbohydrate tolerance, the threshold of which may be passed for considerable periods; in contrast with which, other factors have very slight deviation from normal, (or rather, that the range of variation, both in health and disease, will be very narrow.) This will be illustrated by the constancy of the hydrogen ion concentration of the blood, which variation in normal is not measurable by the usual means, and in disease can vary but a very small measurable amount without causing death; whereas, in these same individuals, the hydrogen ion concentration of the urine may vary from pH of 2 to pH 8, and of the saliva, from pH 3 to pH 7.8.

Another factor that is relatively constant is the calcium present in the blood, which may vary from 9 to 11 mgs. per 100 cc., and is seldom below 9.5 in normal. The calcium present in the urine seldom exceeds 11 mgs. per hundred cc., and in the saliva has a relatively wide range in calcium oxalates and in calcium as oxides. In this supposed patient we have a distinct tendency to rarefying osteitis and calcium absorption, expressed both in radiolucency of bones and reaction to inflammation, both in the mouth expressing itself as periodontoclasia, and in the involved joints as a type of rheumatism. This suggestion of a disturbance of the calcium balance, or of the calcium controlling mechanism, is emphasized by the depressed calcium content of the blood and the increased calcium content of the urine and saliva. While it is impossible, in the present state of our knowledge of calcium metabolism, to affirm which factors are causative to others and which are symptoms as the result of some as yet unknown cause, it is strongly suggested that the calcium disturbance of this case is in part the result of the bacterial invasion of the gingival tissues, and the absorption of toxic substances which are the products of bacterial reaction in tooth structure. For example, we have many illustrations of disturbance of the thyroid from dental infections and other causes. A disturbance of thyroid function may in those cases, be the controlling factor in metabolism, which determines the amount of depression of the calcium balance in the blood, the rate of calcium assimilation of food, state of calcium hunger of the system, expressing itself in part by the taking up of calcium readily from inflamed osseous tissues, and its wastage as overflow in the excretion products; or, as is more probable, both the thyroid and parathyroids may be so involved and so contributing.

We do not present this as a conclusion, but as one of the suggested interpretations of the group of phenomena presented in this case; and this case represents a group, and it will be by enlarging our information of the various individuals in such groups, that we will be most likely to advance our knowledge of this phase of the problem. (One of the hopeful ways of enlarging our knowledge of this and similar types of pathology will be by studying similarly as large a number as possible of individuals grouping naturally into this and other groups.)

When we review the data developed in the preceding chapter, several factors have been greatly emphasized. Rabbits will continue for weeks and months to show a constant calcium without a variation of more than a fraction of a milligram. If within twenty-four hours after a piece of the infected root has been removed from the human, it is placed beneath the rabbit's skin, the ionic calcium of its blood begins to change and the change is progressive and continues unless that animal be capable of maintaining an adequate defense immediately about the tooth. In all cases where the animals have built up such a defense, the local expression has been one of concentration about the implanted piece of a highly vascularized connective tissue; and when this tissue is finally broken down, in those cases in which it is, the systemic defense soon gave way; and, similarly, as the rabbit's condition took on certain characteristics, such as depressed ionic calcium with loss of weight and progressive change toward death, very frequently the patient, from whom that same tooth was extracted, progressively gained in weight, had a progressive change in the ionic calcium of the blood, and lassitude gave way to a condition of well being, etc.; and, similarly, a patient suffering from leucopenia progressively developed an improvement in that factor of the blood, and the rabbits beneath whose skins the tooth or a piece of it was planted, proceeded to develop a leucopenia in many cases. It is, therefore, not an accident that the rabbits, who resisted the infection, practically always built a defensive tissue about the implanted infected tooth.

There is really no way that this relationship between the local and the systemic expressions can be so clearly seen as by watching a dental clinic which furnishes a wide assortment of conditions; for, while it is true that few cases can be said to belong to any one grouping with complete freedom from aspects of some other basis of grouping, the general expressions will be so constant as to emphasize the constancy of these relationships.

CHAPTER XLIX.

INTERPRETATIONS.

INHERITED SUSCEPTIBILITY AND MENDEL'S LAW.

DISCUSSION.

In the four chapters preceding, we have reviewed the phenomena of infection and local and systemic reactions and their relationships to each other. In these we have summarized the researches of previous chapters. In many of these studies and analyses we have found that while individuals are not comparable as a whole, they tend to divide into groups, the members of which are directly comparable. This general tendency to grouping is related directly to the presence or absence of a susceptibility to rheumatic group lesions. In the main, they divide into two groups: Those who are and those who are not susceptible; except that of those who are not susceptible, they may become so, usually temporarily, by overload; and when they do break, the tendency is to break in the overloaded tissues and organs, or the nervous system. The other group with natural tendency to susceptibility we have found to have that quality in common with other members of the same ancestry and with one or both sides of the ancestry, though this quality may be present in a strong or weak degree of dominance. In this chapter we desire to study these individuals and the data of these researches with particular reference to the fundamental laws of heredity, usually spoken of as mendelism or mendelian traits.

Mendel was an Austrian monk, the centenary of whose birth has recently been celebrated, but whose work made no impression upon the generation to which it was given nor for some succeeding generations, and it was not until the great principle was rediscovered that any importance was given to his writing. He found in growing his garden peas that the interbreeding of different types developed new types which had definite relations to the old, and that these followed a law of proportion. This has become so fundamental a part of all the modern thought and teaching of biology that it is generally accepted and taught as being just as constant a law of cause and effect as the laws of magnetism, gravitation, and light. In general, the fundamental tenets of mendelism may be expressed about as follows:

(1) Characters are inherited as units. That is, that my boy has a nose like mine, independent of whether other characters such as hair, eyes, stature, etc., etc., are alike.

(2) Characters are not inherited, but determiners for them are. That is, that my boy does not inherit my nose in any sense but that he inherits determiners which provide for a nose like mine.

(3) My boy does not inherit anything from me that I did not inherit from my ancestry. In other words, that he and I are half-brothers by different mothers, and each one of us has the same, or in part the same, type of determiners that have been handed down through the long chain of ancestry.

These fundamental principles are modified more or less widely for different types of unit characters. For example, some characters are inherited only through the mother's side of the ancestry, as, for example, the quality of color blindness. Others are inherited in equal dominance from both sides of the ancestry. Still others denote the presence of a dominating determiner, such as brown eyes; whereas blue eyes denote simply the absence of a determiner for brown pigment. In still others, one character tends to dominate, while others are in mathematical proportion. To illustrate:

Crossing blue Alsatian fowls with white, will produce an equal number of blues and whites—namely, one-fourth of the total of each of these two colors—whereas one-half of the total will be neither blue nor white but will be speckled; and these speckled fowls will produce the same ratios of blues and whites, when crossed, as will the whites and blues from this same ancestry. Whereas, if white guinea-pigs are crossed with black guinea-pigs, the first generation will be all black guinea-pigs, which black guinea-pigs, when crossed, will contain determiners for both whites and blacks; and in the next generation, there will be three blacks to one white, the black dominating in about this proportion over the white. Important experiments have been made to ascertain the seat or origin of this force in heredity, one of which was to remove the ovaries of a white guinea-pig and in their place put the ovaries of a black guinea-pig. She was then crossed with a white guinea-pig, and, whereas the offspring of all matings of two white guinea-pigs could only produce white guinea-pigs, in this case, the crossing of these two white guinea-pigs, the female of which carried the ovaries of a black guinea-pig, produced only black guinea-pigs. In the next generation these black guinea-pigs carrying the determiners in the proportion of one to three of whites to blacks, would produce one-fourth white guinea-pigs and three-fourths black guinea-pigs. It is, accordingly, established that the determiners are resided in the cells of the sex organs and are transferred from the sex organs of one generation to those of the next generation independently of all other cells of the body.

In the light of these data regarding the laws of heredity, let us review our findings regarding susceptibility and its expressions.

In Charts 43 and 48 we found that there was a very marked tendency for individuals with rheumatic group lesions to produce offspring who tended to be susceptible to rheumatic group lesions. This is so marked, that it becomes directly a means of classification where the histories can be obtained with sufficient completeness. But this is not new. Sociologists have long been furnishing data demonstrating that heart disease, for example, tends to run in the family, and similarly, many other affections; and while our later developments have demonstrated that rheumatic group lesions are quite largely the result of infective processes, this does not change, though it puts new light on the already well established principles as laid down by statisticians. But there is an important new development which has come out of these researches, which, so far as I know, has not been developed previously; namely, that the tendency to rheumatic group lesions of a given type, for example, heart or rheumatism, etc., follows a law that corresponds to this general law of mendelism: namely, *that inheritance susceptibility of various organs and tissues is a unit character so far as different organs and tissues are concerned, as completely as with color of skin, hair, and eyes, length of nose, height of stature,* etc., etc. In other words, we have shown in Chapter 4 that a careful analysis of the lesions of various organs and tissues demonstrates that where they do appear, they appear in large numbers of a family. For example, as shown in seven hundred families, there are more cases of heart affection in one hundred families than in the other six hundred.

CHAPTER L.

INTERPRETATIONS.

AN INTERPRETATION OF RADIATION REACTIONS.

DISCUSSION.

Previously, in Chapter 27, we have discussed researches on the effects of different types of radiation upon normal and pathological tissues. From these it has been shown that when teeth, from the infection of which there is an extensive flow of pus, are exposed to the Roentgen-rays of suitable length, one of the very conspicuous effects is the diminution of the quantity of pus produced, so much so that it is a very frequent experience to see fistulæ of long standing, from apical root infection, close quite rapidly after the raying in even such amounts as would be used in making a few roentgenograms, and particularly so with the former types of tube in which the penetration was very low, much of which radiation was absorbed by the tissue. Our researches disclosed that extensive periodontoclasial lesions, if judged solely by the criteria of pus, were apparently greatly benefited by raying with this type of radiation. Quite different effects are produced on pathological tissue of the mouth, as, for example, periodontoclasia, or pyorrhea alveolaris, with different types of radiation.

We are all familiar with the tanning effect of the sun's rays upon the skin and with the life-giving effect to all vegetable and animal life, which comes from these rays. We have referred in Chapter 27 to the increase of rickets in dark and cloudy countries and areas, and its cure by the subjection to either the sun's rays or to mercury vapor arc radiations.

Early in the history of radiation studies, Finsen discovered that by using large lenses and concentrating the sun's rays and taking the heat out of these by passing them through suitable substances, such as water, these radiations had marked effect on certain chronic ulcerative diseases, such as lupus vulgaris, and also on deeper diseased conditions. Following out and developing this line of work, various types of arc light lamps, including mercury vapor arc, have been and are used to generate rays having lengths approximating those that have been found in the sun to be of marked curative value.

Similarly, radium had been found to possess qualities which are very unique and not entirely unlike those of the Roentgen-rays. For example, probably today more epitheliomas are treated with radium than by any other means, if not by all other means combined; and in the early stages this treatment is almost specific in terminating the tendency to malignant cell proliferation. The only reason that it is used most for cancers of external surfaces is because of the penetration, only a small proportion of the rays passing though to deep layers.

Periodontoclasia, or so-called pyorrhea alveolaris, is a very general term and is applied to a great variety of lesions which are, in the main, different stages of a general process, and the same periodontoclasia pocket in those different stages will furnish as wide a range of type of tissue, as will be found in a rodent ulcer at one extreme and a bee sting in the other; and yet in all its various extreme and intermediate stages, it is thought of, and spoken of, as the same lesion. In its early stages tissues, with great capacity for reaction to irritation, are making a normal and violent effort to resist the attacking irritant, with the consequential effect of all acute inflammations: namely, absorption of tissue, flooding of the area with lymph and leucocytes, which, together, make what is readily considered an abundant flow of pus. Flooding this tissue with rays of the variety of the Roentgen-rays, destroys the capacity of those cells to make that normal and efficient reaction, and the reduction of the pus in the presence of the maintained irritant is not an evidence of the removal of the irritant by the creation of a toleration and lack of reaction to it. True, these tissues may be those of a patient having exalted capacity for reaction, which I will discuss later.

A later stage of this same periodontoclasia pocket is one in which no pus is generated. Incidentally, the bacterial flora in these different stages quite considerably change; but in this final condition of exhausted function of reaction, we have the type of periodontoclasia pocket which does not respond to treatment. In its early stages with its acute reactivity, repair is most gratifying and rapid with removal of the irritant. In this latter condition the patient's health is endangered to a much greater degree, for in the former condition Nature is maintaining a pretty successful quarantine; in the latter, she is not doing this because tissue of low vitality often is related to definitely dead alveolar tissue, (which dead bone is abundantly infected with streptococci which readily enter the system,) and from the old chronic periodontoclasia pocket we may have serious and extensive, though usually not sudden in development, systemic involvements. When tissue in this state is treated with Roentgen-rays and radium, and already depressed cell function is still further depressed, and if results are to be judged by the one standard of flow of pus, even this type of condition may seem to be improved, or at least not to be made worse, while in reality, it has really been made worse. Our researches have showed that when this type of tissue is exposed to radiations of suitable length, there is a very definite tendency to increase the cell activity or reaction capacity of the tissue, with the effect that again there is thrown out the exudate, and again a capacity for repair accompanied by a change of bacterial flora from the chronic stasis of the poorly reacting tissue to that characteristic, or more nearly so, of the active periodontoclasia pocket in its early stages. This, then, becomes immediately a means for observing both the type of pathology involved, and the effect of medication, particularly by means of radiation. My interpretation of these phenomena is that we are dealing with the same problem that we have discussed in the three preceding chapters—namely, types of reaction—and when we can know more about the mechanism within the cells themselves, we can understand more exactly by what means radiation produces its effects.

When the larvæ of flour mites are exposed to radium radiation of the proper amount, the effect is completely to change the life cycle, and the small moth will continue to live in its caterpillar stage, while those of its fellows, which were not exposed to the rays, have passed through three complete cycles of caterpillar to moth. Similarly, when certain plants are exposed to the radiations of radium, while they continue to live, they do so as stunted specimens. Something has happened which radically changes the vital forces within the cell.

Whether these changes which we are considering as result of radiation can be harnessed and made to modify quite largely local tissue reactions, only further experimentation can establish. The evidence to date, however, strongly suggests that great progress will be made along these lines. There are, however, as evidenced in the large number of histories which make up a part of these studies, abundant illustrations that back of the local expression is a very definite systemic capacity, which relates not only to this individual, but to many or most of those having the same ancestry. We are dealing, then, with forces which are variable and which, while subject to influence by forces which sift and mold Nature's fundamental potentials, tend largely to follow the order of their kind.

CHAPTER LI.

INTERPRETATIONS.

THE PHENOMENA OF SENSITIZATION REACTIONS.

DISCUSSION.

In Chapter 30, we have discussed the quality or symptom of anaphylaxis or tissue sensitization. We called attention to the common illustrations of this condition known as hay fever, asthma, and certain skin disturbances. We also demonstrated that similar conditions may be and frequently are produced by dental infections. By reproducing these symptoms in animals, we demonstrated that we were not dealing necessarily with bacterial invasion. For example, the filtered washings of the crushed teeth of a patient, suffering from a violent inflammatory process of the nose and air passages with acute inflammation of the eyes, accompanied by bloodshot and extreme lacrimation, were injected into rabbits and produced in forty minutes a similar bloodshot condition of both eyes and acute rhinitis. This reaction occurring in forty minutes is, of course, not an anaphylaxis.

While the studies of sensitization reactions have not advanced so as to furnish a definite conception of the mechanisms involved in this reaction, they have been carried far enough so that the interpretation of many of the phases are quite generally accepted. Some of these are that there is a reaction between antigen and antibody; that this antibody does not exist natively in most animals, but that it is created by the first injection or entrance of the antigen in question into that animal's system, and that this process of reaction which creates the antibody, which latter unites so violently under certain conditions, if the same antigen is introduced, is closely related to the process known as immunity. To illustrate:

If most any protein as, for example, egg albumin, blood serum, tissue extract, or milk, is injected into the circulation in even a small quantity, or even in a relatively large quantity, it will produce no effect. If, however, a small quantity of this same protein is injected into the blood stream or tissues of this animal, after a period of six to twenty-eight days, a violent reaction occurs which in many animals terminates in a few minutes in death with spasmodic contractions of the bronchioles, but with a definite chain of symptoms beginning with excitability, then irritations of the nose and skin, then labored breathing, and finally with a dyspnea produced by the maintained contraction of the bronchioles, the heart going on beating for some minutes after breathing is stopped. This reaction may be produced by the introduction into the system, as a first or sensitizing dose, of a quantity of material incredibly small. One millionth part of a gram, as a first or sensitizing injection, will suffice to induce that animal to develop the antibodies, which latter will react very violently with this same protein antigen, if introduced after the incubation period. This condition of maintained ability to react, compares in many ways with the ability to react to a second invasion or exposure to a contagious disease, to which the individual has by the first exposure to an infection built up a capacity for reaction, which we speak of as immunity.

Similarly, individuals become sensitized to proteins which enter the body not only through the air passages, as in hay fever, but from ingested foods. Not infrequently, in fact very frequently, individuals are sensitized to egg, milk, banana, certain cereals, in fact almost any food product; and in this case, it is believed that the alimentary tract allows some of this unsplit protein to enter the system in sufficient quantity, to be acted upon by the antibody that has been developed by the previous entrance into the sytem of that protein, and all that is needed to cure this sensitization to a given food product, is to eliminate that food product from the diet, just as individuals subject to hay fever have only to protect themselves from the particular pollen to which they are sensitive by going to a community where that species of plant does not grow. Accordingly, individuals living on limestone belts find relief in going to areas with laurentian formation where the flora will be entirely different.

In the case discussed in Chapter 30 in which the patient suffered from a violent rhinitis and coryza, we found that he was acutely sensitized in other tissues, as well as those of the nose and throat, to the toxic substance extracted from his teeth, and that the violent and frequent attacks entirely disappeared with the elimination of his dental infection. We are then, apparently dealing with a substance which obeys the classical expression of true anaphylaxis. If, however, sensitizations express themselves in a large variety of forms as we outlined in Chapter 30, and in many, if not all, of which the dermal reaction is efficient in demonstrating them, why is it that individuals in perfectly normal health do not respond to dermal tests for sensitization and individuals with other forms of affections such as some of the rheumatic group lesions do respond to dermal reaction tests quite as effectively as those with the classical symptoms of sensitization, such as rhinitis, asthma, etc.? One of these two things obtains: either the classical rheumatic group lesions are in part forms of sensitization reactions, or there is a strange coincidence in these individuals' reacting contrary to the accepted significance of dermal reaction. To determine the presence in the body of an efficient defense for diphtheria, the Schick test is administered which is a dermal reaction test for that sensitization; similarly, the tuberculin test, the Abderhalden test, etc. We will discuss this further in the chapter on the mechanisms of local and systemic defense.

In Chapter 30, I discussed the fact that individuals may develop either or both a primary or secondary reaction to the skin test. The significance of these two and the mechanisms on which they are based are probably somewhat as follows: The first reaction seems to be a true allergy and consists of the reaction of the antibody with the antigen, and seems to be related only to the passage through the system of a toxin antigen produced by bacteria in some tissues of the body. This primary reaction frequently appears in thirty seconds; is unique in its characteristics, consisting of a central raised wheal surrounded by a zone of marked erythema, which frequently outlines the courses of the subdermal chains of lymphatics. It reaches its maximum usually in from fifteen to thirty minutes, and frequently within an hour is conspicuously disappearing, and may be quite lost in two hours. Occasionally this primary reaction may last three or four hours. In certain individuals there will appear at the site of this same test a secondary reaction beginning in from twelve to twenty-four hours. It may last from a few hours to several days, and in some instances there may be a considerable breaking down of the central zone. In the primary test there was a central white spot constituting the raised wheal. In the secondary reaction there is no raised central wheal, the erythematous zone extending from the center to the periphery, and most intense in the center.

The significance and nature of this secondary reaction is important. Whereas the primary reaction was dependent entirely upon the presence in the system of a protein toxin without the presence of bacteria, the latter or secondary reaction seemed to indicate the presence in that system of the bacterium itself apart from, and in addition to, the toxins of the bacteria. We have, then, in the patients reacting only to primary sensitization evidence of a toxic irritation without bacterial invasion and in the latter evidence of a bacterial invasion. When both appear, both are present. When the second appears, it is our experience that, practically, always the primary is present. In the case referred to in Chapter 30, it will be noted that this patient was tested with three antigens, prepared in different ways, all of dental origin. This patient gave the primary reaction to all three of these antigens, but gave the secondary reaction to only one. We conclude, therefore, that he was suffering from a bacterial invasion of the body from the dental infection in addition to the toxin invasion. We have, then, by this procedure, what seems to be a means for determining whether an individual is suffering from either or both a toxic absorption from a focus or a bacterial invasion from it.

SUMMARY AND CONCLUSIONS.

This work that we are presenting here is, we consider, very important. But this shall be considered as a preliminary report as we are carrying forward these investigations and will have additional data to present later. These involve methods for the application of this principle in dental diagnosis and its application in making various determinations.

CHAPTER LII.

INTERPRETATIONS.

INTERPRETATION OF SEROLOGICAL STUDIES.

DISCUSSION.

In Chapters 19 and 20, I have presented researches conducted to determine something of the changes that are produced in various sera of the body by dental infections, in which we found some very marked results. For example, a patient suffering from hemophilia not only was relieved himself by having infected teeth removed (a most difficult process in his extreme condition for he was nearly dead from spontaneous hemorrhage chiefly from the gums but also from the nose, and was deaf in one ear from spontaneous hemorrhage in the internal ear), but cultures from these teeth, when inoculated into rabbits, produced similar changes, in many of which the clotting time was greatly lengthened and in several, spontaneous hemorrhages developed. One of these died in twenty hours with many spontaneous hemorrhages throughout its body, as shown in Chapter 60.

Similarly, we have seen marked secondary anemias rapidly improve after the removal of dental infections. (See Chapter 60 on Anemias.) So definite are these effects in some instances, that even the transfer of the infected teeth from the patient suffering from acute nephritis to a position beneath the skin of rabbits, has produced in several instances acute nephritis in the rabbits as shown in Figure 203. Not only can these conditions be produced by the introduction of the organisms, which have been grown from the infected teeth, but changes may be produced in the various sera by the introduction into the animal's body of the toxic substance extracted from teeth separated from the bacteria themselves. This is demonstrated in Chapter 17.

It seems to be proved that dental infections can be the chief causative factor in many of the disturbances which express themselves as changes (or in changes) of the various sera of the body. Whether or not these changes occur by direct reaction between the toxic substances developed by the teeth and the contents of the blood stream, either by disturbing the functioning of the glands of internal secretion, or as sensitization processes, either directly upon the vital fluids of the body or the tissues producing them, we are unable to state from the information available. It seems probable, however, that several of these forces are at work, and we must wait for much more research data before an interpretation can be made of these phenomena.

CHAPTER LIII.

INTERPRETATIONS.

THE RELATION OF GINGIVAL AND APICAL ABSORPTION TO SYSTEMIC DEFENSE.

DISCUSSION.

In Chapter 4, we studied the similarities and differences routinely expressing themselves in various individuals, which, in general, indicated that while individuals are not, in the main, comparable, the characteristics are sufficiently definite to use them as a basis for classification of those falling within different analagous groups.

In Chapter 3, we found that the local expressions of infection in bone about the teeth tended definitely for a classification of individuals into those with extensive absorption and those without. These differences were also found expressed in bone reactions in animals.

In Chapter 5, we discussed the gross relationships between local and systemic reactions and found not only that individuals can be classified according to these two methods of study, but that the classifications include not only, in general, individuals of the same groups, but the striking illustrations are the same individuals for each of the two sets of groupings. To illustrate: When we divided individuals into groups, selecting those who had the most extensive rarefaction about dental infections, and again made studies to determine the individuals that were without systemic expressions from dental infections, when such were present, our typical illustrations were the same particular individuals; and, similarly, when we selected the individuals with least reaction for a given dental infection, they proved to be the same individuals that we had selected as most strikingly significant of the group with marked susceptibility. Note that we said "*Least reaction for a given dental infection*" which is very different from saying individuals with the least infection. Considering these two conditions as representing extremes of local reaction on one hand, and systemic susceptibility on the other, we found that intermediate groups had similarly definite characteristics. Thus a lateral tooth with a putrescent pulp would, in the individuals with absence of systemic susceptibility, be attended by very marked apical absorption and a fistula; in the individuals with low defense, very slight absorption and no fistula; and in the individuals with, ordinarily, a high defense but which defense has in recent time been broken by overload, there would be evidence of a zone of moderately extensive absorption, evidence of a healed fistula or none at all, or a zone of condensing osteitis surrounding the zone, made radiolucent by the rarefying osteitis.

In Chapter 8, we studied the relation of gingival infections to pulp infections and found that, in practically all cases of extensive gingival infection, the pulp is already involved, and in cases with moderate gingival infection, frequently so.

In Chapter 10, we studied the relation of gingival infection, or periodontoclasia, to systemic disturbance and found what seems to be an almost complete contradiction to the teaching and expectation of the professions, for instead of the dominance of gingival infections progressing in the order of systemic susceptibility, it tended, when considered in its acute forms, to be in precisely the reverse order, for, in separate studies compiled for me from my records by different members of my staff, the remarkable data came out that, in the cases of marked systemic susceptibility to rheumatic group lesions, practically no cases of acute periodontoclasia in the active stage were found; and, conversely, in the groups with high defense to rheumatic group lesions, frequently this type of disturbance was present. These are clearly brought out in Figures 85, 86, and 87 of that chapter.

In Chapter 11 we found by comparing gingival absorption with periapical absorption and tendency to caries, that with a given dental infection, let us say the amount that would be involved in putrescent pulps, the extent of the apical rarefaction tends to be in direct proportion to the susceptibility to gingival absorption to gingival irritants, clearly demonstrating a direct relationship. Not that either is causative to the other, but that each is a symptom or effect of the same causative factors.

In Chapter 12, we found that the extent of the absorption is rather a measure of the defense than a measure of the danger.

In Chapter 13, we found that the discharge from a dental fistula does not contain, ordinarily, large quantities of living organisms, as has been generally supposed, but contains very few, and such as are found are nearly all digested or phagocyted; that the discharge is made up almost entirely of blood plasma, leucocytes, and neutralized products.

In Chapters 45 to 56 inclusive, I have undertaken to interpret the phenomena in the light of this new information and have presented, for your consideration, that local reaction not only determines whether the patient is or is not relatively safe from his own focal dental infections, but also determines the physical conditions surrounding that dental infection as evidenced by the tissue changes.

If gingival absorption, and the same is true of apical, is, in large part, an effect of vigorous local reaction in Nature's effort to establish a quarantine and defend the patient, it should be possible for us to establish evidence that this reaction is definitely defensive in character. In Chapter 30, in our study of sensitization, we found that the toxic substance extracted from an infected tooth, in some instances prepares animals to be more violently attacked by the organisms grown from that tooth; that these animals were sensitized, as evidenced by dermal reactions, to both the toxic substance itself, if injected after six days, a true allergy, and to the toxin extracted from both the organisms and the artificial media in which they were grown. We also demonstrated patients sensitized acutely to their own dental infections in a variety of ways, one of which was accompanied by rhinitis, coryza, extreme headache, etc., which symptoms were entirely relieved by the removal of the infected teeth; and also that these patients have a very marked dermal reaction to the toxin extracted from their teeth.

We, therefore, may use this dermal reaction as a direct means for determining the presence or absence of this antigen in the tooth substance and in the product of the active local reaction: namely, the pus from the periodontoclasia pocket of that individual. To do this, we have made an extract of the toxin of the pus from the periodontoclasia pockets of the patient with very high defense whose roentgenograms are shown in Figure 262 of Chapter 46, and whose case is reported there in detail, and have found that whereas he did not have either a primary or secondary reaction to the toxic substance extracted from the pus taken from the periodontoclasia pockets, which was very abundant, he did have a definite reaction to the toxic substance extracted from the teeth, secured simply by breaking up the teeth and washing the pieces in a slightly alkaline fluid. The fluid about these teeth was also alkaline and the teeth were, as it were, steeped in it more effectively than by the process by which we made our extract. It is my interpretation at the present, that the blood plasma in which these parts were so abundantly bathed carried an efficient supply of antibody to neutralize this antigen. While we do not yet understand the mechanisms of immunity, it seems very probable that there is significance in the fact that this patient's blood calcium is above the normal, which problem we are discussing in the next chapter.

This would seem to give an entirely new meaning to certain forms of gingival infections. Whereas we have in the past looked upon them as being evidences of a particular type of bacterial invasion or a bacterial invasion working in a tissue that is particularly prone to degeneration, the evidence now would lead us to conclude that there is inherent in the body, probably directly related to calcium metabolism, a mechanism of defense which adapts itself to tissues in all parts of the body, and which is a definite part of function of the hematogenous and lymphogenous circulations. In all tissues embarrassed by a threatened approach of bacterial invasion, there is, then, in these fluids, a force which manifests itself vigorously, and therefore efficiently, at the root apex. The problem is not unlike that at the gingival border except that there is no other means of escape for the bacterial and toxic substances than into the blood stream until Nature shall, by this activity, blaze a way to the surface as an apical fistula, and there, with a stream of neutralizing fluid, carry these invading products to zones outside of the body, for in this sense the alimentary tract is outside of the body and is so considered in biological studies, and this is Nature's quarantine. The price we pay for it is the destruction of alveolar bone, whether at the gingival margin or the apex, but it is abundantly worth the price. In succeeding chapters we will apply this interpretation to other types of infection.

This explains so many things that have been conundrums in the past. For example, why is it that the same condition, produced by a gold crown forced into the gingival tissue, will in one case produce so much absorption and inflammation, and in another the tissue makes little or no outcry against its presence? Or again, food is packed between teeth where the contact points have been lost. In one instance, the absorption of alveolar bone has taken place nearly to the apex; in another, the food is jammed against the tissues, week after week, with little or no local reaction. Not that the tissue is not injured and infected. It is, and that's the pity of it. Or again, why is it that in some mouths a tooth with an infected pulp produces almost no local disturbance about the tooth, while in another if it does not have a fistula, it recurringly is very painful or tender? Apparently, in the light of these studies, in the latter case the reaction process is directly the measure of both the discomfort (which is incidental to the second) and a successful defense against systemic disturbance, while the tooth without this reaction not only is not painful but unlike the other, which will be easily extracted, it is very difficult to extract.

CHAPTER LIV.

INTERPRETATIONS.

THE RELATION OF LOCAL TISSUE REACTION TO CALCIUM METABOLISM.

DISCUSSION.

This is a problem regarding which there is very little in the literature; which does not mean that it is not very important but probably does indicate first, that it is a very difficult problem to study, and second, that it has not attained the prominence and importance that it seems destined to, in the studies of immunity and susceptibility.

In Chapter 19, we have studied serological changes in the blood produced by dental infections. In Chapters 19 and 20, we have discussed the marked changes in the various sera of the body, produced by dental infections. These have demonstrated that several of the factors involved seem very definitely to be related to calcium metabolism. For example, in Chapter 60, we have revealed a case where the patient was suffering from very acute hemophilia, which condition was greatly improved by the removal of his infected teeth, the cultures from which infected teeth, when inoculated into rabbits, not only produced striking changes in clotting time, but, in Chapter 60, there is shown a rabbit which bled to death from spontaneous internal hemorrhage within twenty hours after being inoculated with this strain, and there was not enough blood left in the heart and blood vessels to make a chemical analysis, which is frequently done. Similarly, the clotting time of many of these rabbits was delayed as was the patient's. This patient's total calcium was down to 8 mgs. where the ionic alone should be above 10.

In the various studies preceding this, we have been analyzing gradations in rarefaction of bone, both locally as a zone of absorption and a reduction of the total lime salts producing a radiolucency to the Roentgen-ray. These researches have shown that in most patients with a marked susceptibility or low defense, there is a marked increase in deposition of calcium, associated with condensing osteitis, and in individuals with a high resistance and low susceptibility, there is a marked tendency to a reduction of osseous tissue with rarefying osteitis. In Chapter 34, in studying the effects of pregnancy, we found that during this period of calcium stress, as in the period of lactation, there is a marked susceptibility to rheumatic group lesions. The state of calcium hunger which obtains during periods of over-demand for calcium, as in pregnancy and lactation, seems clearly to be influenced and aggravated by the presence of streptococcal infection, such as dental infections.

The evidence at hand would seem to suggest that in most cases it is not so much the presence or absence of an available supply of calcium, such as calcium bearing foods, as it is a disturbance of the mechanism which governs calcium metabolism. In the subsequent chapters, in which we study in detail the individual cases, we have many instances suggesting a direct relationship between thyroid and parathyroid activity, and calcium metabolism and dental infection. That local tissue reaction is directly connected with calcium metabolism there seems no doubt. What this relationship is, and the means whereby local and systemic defense may be strengthened by modifying calcium metabolism, is not yet clear, but it is a problem of supreme importance and its study promises most favorable and important results for expended effort.

When we associate the relationships between the clinical conditions of the individuals and their ionic calcium, we find a very strong suggestion of relationships between cause and effect, and these are more strongly brought out when we review in connection with these clinical and chemical data, some of the determinations made *in vitro* and by animal experimentation with dental infections. Some of these are:

(a) *Individuals, with dental pathology of a type which expresses itself with liberal destruction of alveolar bone, whether at the gingival margin or at the apex, have at the time that process is active, generally, if not invariably, a normal or high ionic calcium of the blood; and, conversely, individuals, with a tendency to the development of deposition of calcium, as condensing osteitis, tend to have a low ionic calcium of the blood at the time that process is active.*

(b) *Individuals, with a marked tendency to dental caries, have at the time of the activity of that process, very generally, an ionic calcium of the blood below normal; and, conversely, individuals with complete freedom from caries almost without exception have an ionic calcium of the blood at or above normal.*

(c) *Individuals, with a low ionic calcium of the blood as a persisting and normal condition, tend to have much more dense and less permeable supporting structures for the teeth, as evidenced by the difficulty of producing anæsthesia; and, conversely, individuals with normally a high ionic calcium of the blood tend to have a condition of the supporting structures which makes them quite easily infiltrated with local anæsthetics.*

(d) *Individuals with a low ionic calcium of the blood tend to make a slow repair, with marked tendency to secondary infection of sockets following extraction; whereas, individuals with a high ionic calcium tend almost invariably to have a rapid repair, without tendency to secondary infection following extractions.*

(e) *The phenomena of the so-called dry socket, with its painful secondary infection following extraction, is almost exclusively limited to the individuals who, at the time or previously, and generally both, have a low ionic calcium of the blood.*

(f) *Radiopaque bones of various parts of the body tend to be associated with a chronic state of lowered ionic calcium of the blood; whereas, radiolucent bones tend to be associated with a high ionic calcium of the blood. The extreme forms of this which become pathologic, as osteomalacia, emphasize this same relationship.*

(g) *Individuals, with a low ionic calcium of the blood and with the consequent or associated condensing osteitis occurring about infected structures, tend to have the formation of sequestra; whereas individuals with a high ionic calcium rarely do so.*

(h) *Individuals with a high ionic calcium of the blood tend regularly to develop periodontoclasia and alveolitis as a reaction to local irritations; whereas, patients with a low ionic calcium do not tend to have this reaction.*

While it is exceedingly important that we shall visualize, even though imperfectly, somewhat of the role of calcium in metabolism and disturbed function, the problem is rendered doubly difficult by the fact, that incomplete statements, while in the main correct, will be read as complete statements; and I will ask that those who read this keep in mind continually that I am simply undertaking to associate the data that have been revealed in these researches and am suggesting what, in the light of the present knowledge, seems the most logical explanation. Some of these important relationships to be considered are:

(i) *When infected teeth are placed beneath the skins of rabbits, there is practically always a reduction of the ionic calcium of the cir-*

culating blood, which ionic calcium decreases progressively as death is approached, which generally occurs between six and seven milligrams.

(j) *When some infected teeth are placed in normal blood, this change in ionic calcium is rapidly produced.*

(k) *The pathologically combined factor can be determined and the bond with the toxic factor broken.*

We seem justified in suggesting the following as brief expressions of the role of calcium in life and metabolism:

> **1. Cellular function, whether hypo-, hyper-, or dis-function, is affected, if not directly controlled, by the concentration of ionic calcium in the bathing fluids.**
>
> **2. Life in every form seems to be dependent upon free ionic calcium in the pabulum in which it exists.**
>
> **3. The vital capacity and vital efficiency are both inseparable from, and dependent upon, calcium metabolism.**
>
> **4. While the role of calcium in vital processes is of supreme importance, its presence or absence is probably not the primary and chief factor in cell function, since there are certain pathological states in which the calcium present is not of the order just stated, but one in quite direct confliction with these general principles.**

CHAPTER LV.

INTERPRETATIONS.

THE MECHANISMS OF LOCAL AND SYSTEMIC DEFENSE.

DISCUSSION.

The science of immunology has not been developed far enough for the factors involved to be definitely segregated and interpreted. If we would undertake to summarize the eight preceding chapters and express the conclusions made in them in a generalization, it would be about as follows: Since I interpret local reaction to be the most important characteristic of local dental infection, and also that systemic defense against dental infections is a measure of ability of the system to establish an active local defense at the point of focal infection, together with an adequate defensive mechanism for each and every organ and tissue of the body, therefore immunity has, as one of its fundamental factors, a capacity for intracellular defensive reaction.

Our studies of the phenomena of sensitization, as applied to this problem, indicate that this condition plays a very large part in both a successful defense against dental infection and a sensitization to products of dental infection origin; and, also, that there is a direct relationship between anaphylaxis to dental infection and immunity against dental infection. Not that these are similar, but that they are closely related factors. Indeed, it seems probable, that in a very important degree or manner the disturbance which we recognize in one individual as a true type of allergy, with rhinitis, coryza, etc., is not unlike, except in manifestation and involved tissue, the reaction in synovial membranes, heart valves, kidney, etc. When antigen meets antibody, the reaction is intracellular. When the sensitized tissue, prepared for defense by its sensitization with its attached and occluded antibody, receives its arch enemy, the antigen which produced that sensitization, there is a violent local reaction with ischemia, hyperemia and distention, and often edema. If this reaction be violent enough, there is necrosis, which condition often follows our secondary reactions. A part of this process involves not only throwing into the tissue of the products of necrosis, but into a tissue whose mechanism for repairing damage and removing waste has been disturbed or destroyed, either permanently or temporarily. We have, then, a localized necrotic process in an otherwise perfectly normal tissue.

Our studies have shown that the presence of the toxic substance taken from the teeth inoculated into animals frequently makes them more susceptible to attack by the organisms which produced that toxin. If, then, applying this to the local tissue, when the organism which produced the toxin is wandering through the system, having gone beyond the quarantine of the focal infection, where will it find its pabulum? It would seem most likely that it would be in tissue whose local defense has been destroyed by this *antigen antibody reaction* and which chemically and mechanically has been deprived of its local function for defense. There is also a pabulum of necrotic tissue for this organism; and the heart valve, synovial membrane, or kidney tissue becomes a prey to the dental infection. This may be only a theory, but we must have some visualization from which to start, and whether this be correct or incorrect, and there is much to suggest that it is largely true, it at least makes a starting point; and if this bridge across the chasm be not adequate to carry the entire responsibility of interpretation, it, at least, may serve as a temporary trestle until we can rebuild it with a more permanent structure.

In support of the hypothesis that I have just presented my researches have brought out among the important new data the following:

(1) Individuals with a high defense to the rheumatic group lesions seem, almost invariably, to have a high ionic calcium of the blood during and preceding that state of high defense.

(2) The ionic calcium of the blood seems definitely related to the capacity for reaction as expressed in the supporting structures of the teeth which have been injured by irritation, either gingival or apical.

(3) Individuals presenting with sensitization reactions of the type of allergies of the mucous membrane, skin, and special tissues, all have a high ionic calcium and a high pathologically combined calcium, and belong to the group which we would classify from the type of pathological changes in the injured supporting structures of the teeth, as having an acquired susceptibility.

(4) (a) Anaphylaxis from dental infections seems definitely to

be related either to a long continued state of reactivity, in which process certain tissues take on a hypersensitization; or (b) a reaction occurs as the result of the pathologically combined calcium or some other factor in a system whose normal defense is sufficiently high (and there is still available a normal ionic calcium in these cases) to prevent its expressing itself in joints and muscles and organ tissues, since these individuals with anaphylactic reactions to dental infections seem never to have the dental infection express itself as rheumatism, heart involvement, or neuritis, etc.

To state this last observation differently, if the systemic reaction to the pathologically combined calcium (assuming that the dental toxin is in combination, as our evidence seems to indicate, with a portion of the ionic calcium of the blood) occurs in an individual with high total calcium, or at least with a still sufficiently high ionic calcium to be practically normal, say 10 to 10.5 milligrams per 100 cc. of blood, the systemic reaction is liable to take the form of a sensitization which is similar to, if not identical with, the classical anaphylactic reactions of tissues to proteins. But if the reaction of the system is to a pathologically combined calcium which is definitely below the normal, that individual does not tend to have the classical anaphylactic symptoms, but does tend to have the usual rheumatic group lesions. There is evidence which strongly suggests that very many disturbances are modifications of anaphylactic reactions, for even those reactions taking place below the normal ionic calcium of the blood have many characteristics which, while they would be clearly distinguished from the classical anaphylactic group, do seem to be the result, in part, of sensitization processes in joints, muscle tissues, organ tissues, etc. Further, it now seems very probable that many of the reactions of the nervous system are in large part a type of sensitization reaction in those tissues, which may affect either motor or sensory groups or the central nervous system; and, indeed, the evidence strongly suggests that disturbed mental states, ranging from fear and discouragement or ordinary blues, insomnia, etc., on the one hand, to the serious mental disturbances such as dementia, mania, loss of memory, etc., may all be, in part, a type of sensitization reaction within the nervous system.

There is also evidence, as I have indicated in Chapter 31 on Dental Infections and Precancerous Conditions, that this state of exalted reaction to dental infection seems to be definitely related to chronic irritations such as erythemas, dermatoses, epitheliomata, warts, and moles, all of which are shown in the preceding and subsequent chapters to have definite relation, in some instances, to focal and dental infections, and completely and promptly disappear with the removal of the dental infections. I would therefore suggest as a possibility for consideration and for careful observation that, since cancer, for example, of the stomach tends to develop in the scars of old stomach ulcers, and since stomach ulcers are so definitely produced by strains having that elective localization when taken from teeth of patients suffering from stomach ulcer, and which disturbances in the patients in many instances, as shown, completely disappeared with removal of dental infections, and also since cancer is so distinctly on the increase, as are also focal dental infections, because far too many teeth are crowned, root-filled, and bridged, which teeth are thereby tied into the patients' mouths and cannot be exfoliated, nor have they their natural vent through the pulp canal, which, though not a safe safety valve, would do one of two things: either make the tooth so uncomfortable that it would have to be eliminated, or make an exit for the toxins of the tooth infections into the oral cavity instead of the patient's system: therefore, dental infections must be considered under suspicion of an indirect association with the causative factors of cancerous conditions. In support of this last observation I would call attention to the fact, that in our fourteen hundred more or less complete family histories, from which we have used approximately one-half as being sufficiently complete and dependable to be worthy of making deductions from, we have found that in the two groups, those with a distinct family rheumatic group tendency and those with a distinct high defense in the family, the appearance of cancer seems definitely to be in larger proportion in the group with natively a high defense and evidence of a break in that defense; in other words, an acquired susceptibility to rheumatic group lesions, which is the same group in which we have found, practically, all of our cases of anaphylaxis. May there not then be some direct relationship between these important facts? In other words, may it not be that the tendency to the development of cancer is directly related to that type of tissue reaction which, for want of a better classification, we are grouping as an anaphylactic reaction. As an illustration of this relationship, I would cite the following clinical case:

Case No. 1351.—A patient with a skin sensitization gave a history of five cases of death from cancer in the family, four on one side of the ancestry. She, herself, was suffering from a heart lesion, from which her father had died and her mother was suffering. Following the extraction of an infected tooth, the reaction upon her heart was almost like an anaphylactic shock. Coming on some hours after the operation, it was therefore not related to the anæsthesia. It was, however, so profound as to make her bedridden, with much prostration, for approximately a week. Before and since that experience, while her mitral leakage places a limitation upon her activities, she has been able to carry on regular duties, and except for her limitation from overloads, leads a practically normal life. Unfortunately, this illustration carries, by inference, a suggestion that I am associating heart involvements with cancer. This is not my belief except as a sensitization process, which may be superimposed on an organic lesion, associates these in this individual.

I would, therefore, briefly summarize these relationships as follows:

> **1. Since the defensive mechanisms, which protect the tissues of individuals, reside primarily in the unit tissues of the body, hyperactivity of those mechanisms constitute phases of pathological states; and, in consequence, many of the acute involvements have their beginning in that state of hyperfunction.**
>
> **2. Some of these processes are true antigen-antibody reactions, which antigen is of focal origin.**

CHAPTER LVI.

INTERPRETATIONS.

NEW LIGHT ON THE PHENOMENA OF IMMUNITY AND SUSCEPTIBILITY TO DISTURBANCES FROM STREPTOCOCCAL INFECTIONS.

DISCUSSION.

The data developed by the various researches herewith reported, together with their application in about two thousand clinical cases reviewed in the succeeding chapters constituting Part Two, have completely changed my visualization of the phenomena of infection and immunity from dental infection sources. My interpretation had been based upon the fundamentals that I have presented as the problems for these various researches. A first change has come in my visualization of the role of the infecting organism. I now see it as a potential force, capable of adaptation through a range and to a degree entirely beyond my previous conceptions. When we inoculate either blood serum or the body lymph with a quantity of the mixed flora of the mouth, frequently no organisms will be found except streptococci and diplococci, with occasionally staphylococci, and these may require a slight modification or dilution of these sera; and, indeed, their growth will depend upon the relative volume of the inoculating dose and the health of the individual or animal.

As I now visualize it, every organ of the body furnishes to the blood stream some element or elements which constitute, or contribute to, the maintenance of the defense of that organ against invasion from these serophytic organisms, for they are practically the only organisms of those ordinarily contaminating the oral cavity. which can grow in these fluids. If any organ or tissue of the body become diseased and fail to furnish to the blood stream its quota of the defensive complex, the circulating media of the body—namely, the blood and lymph—will bring a defective defensive environment to the organism in any focus of that host's body. Their phenomenal capacity for adaptation seems to assist them in developing an attack for that defenseless tissue.

In this connection it must be remembered that an injured tissue or organ is not necessarily one with its defensive mechanism reduced, but is frequently one with its defensive mechanism called into play; and, consequently, the injuring of a tissue or organ in some part of the body will not necessarily call forth a localization in that tissue from a chronic focus; but, on the contrary, that hyperactive tissue has an abnormally high defense unless and until some of its tissue becomes hypo-active and necrotic.

But this state of diminished defense in some organ or tissue is not limited to the processes of degeneration, but it seems demonstrated that this quality, which constitutes a complete protection for a given organ or tissue, is an hereditary one; and, just as the eye may be developed without the brown pigment, so an organ may be developed without its complete defensive mechanism, probably some enzyme or other chemical elements. Consequently, in an individual, who by inheritance finds himself without his normal defense in any given organ or tissue, there is a predisposition for a focal infection, if it exist, to invade that apparently normal, but partially defenseless, tissue. Consequently, a very large number of individuals carry from birth the text of their death certificate, for the principal chapters of their life history of ill health and complaints are already determined, if not written. It is no accident that there are more deaths from heart in the families recorded in our case histories in 16 per cent of our studied cases than in the other 84 per cent. We must think of individuals continually in the light of their defensive mechanisms.

But defense spells reaction, and reaction battle, and battle the products of warfare. This completely changes my visualization of what takes place about the root of an infected tooth. Instead of the record's being one of quantity of soldiers on either side in the contest, since all the soldiery may be at rest, the local story is one of the nature of the combat. But we have known so little of that combat that we have continually mistaken effect for cause. It is not an accident that the strong man dies with typhoid fever or pneumonia, and the weaker man survives. The thing that has killed the former and not the latter, has been that his capacity for reaction has been so great and so suddenly developed that he has overwhelmed his own body with the products of that warfare. It is the patient with a high defense that is made violently sick with fever and prostration from an abscessed tooth; but he or she is soon over it. The individual with low defense has neither the profound local disturbance about the tooth, with extensive swelling from acute dental infection, nor the profound systemic depression. A chronic infection in these two types of individuals will represent two quite different relationships between host and invader. In the individual with high defense, the invader is held at bay with a quarantine which is inviolable, which exists between the invader and the body of the host as a so-called granuloma and its highly vascular mechanism with defenses in excess of all possible attacking force that may be brought to bear by the invader. In the other individual, however, with the low defense, this tactful invader is able to live as a parasite on the pabulum furnished without calling forth antagonism and defensive activities of the host. In this state either or both the toxin or the bacterium may pass the sentries and reach various structures of the body, and in doing so succeed in developing degenerative and destructive processes.

In the history of warfare between units of people, it is always the practice to overwhelm and destroy the defensive mechanisms, such as forts, ammunition trains, etc., as a first requisite for the plundering of the conquered. What could be more subtle than the devices that we have shown to be used by the organisms in dental infections? They reside in a blockhouse within the domain of the invaded host. The boundary, which separates the non-vital dentin of a pulpless tooth from the vital cementum, is virtually an impassable barrier to both the bacteria within the tooth and the mechanisms of defense of the host. There is only one kind of patient that can ever destroy the organisms in the infected tooth, and these I have shown to be only those who have so high a vital capacity that they can carry their immunizing line of defense right up to the tooth and, while combating its toxic substances, proceed piece by piece to take the tooth down by a process of absorption, and, in taking it away, uncover and annihilate the various invaders that are seeking to destroy it.

But that is not all. While this boundary is an impassable barrier to both the bacteria and the defensive mechanisms of the host, our researches have shown that it is a permeable membrane which permits nutrition to pass to the organisms in their protected position. It is as though a den of desperadoes were supplied pipe lines and conduits, carrying into their impenetrable fortress a continuous supply of bread, butter, and meat, and all the requisites for a most vigorous life cycle.

But even this is not the most tragic phase of the combat. From this protected position these organisms may furnish, and seem inevitably to furnish, to every individual who does not maintain that adequate and supreme defense, a toxic substance which paralyzes the very soldiery with which the defense is maintained. In Chapter 41, Variations in the Defensive Factors of the Blood, and in Chapter 17, Quantity, Systemic Effect, and Tooth Capacity, and in Chapter 18, Studies of Pulpless Teeth, I have shown that the leucocytes are the fundamental defensive mechanism of the body and that they may be paralyzed so completely as to be incapable of function, by toxic substances given off by infected teeth, without the presence of apparently a single organism within the system; and, further, that every individual carries an index, which is available for reading, as to what his or her factor of safety is against streptococcal infection, for just as a study may be made of an army to determine its number of soldiers, the number of guns, the efficiency of its marksmen, and the reserve supply, just so the various defenses of any individual's body may be determined in quite general terms by a study of the defensive capacity and mechanisms of that individual's sera.

When a dental infection or any other infection develops within the body of an individual with high defense, the process, as I see it now, is about as follows: A few wandering streptococci will reach the body fluids, whether the blood, its serum, the lymph, or the cellular elements of various tissues. The first combat is largely a quantitative and mass action process. If the total infection be large, local tissue, whether body fluids or organized structure, may be overwhelmed, or the trauma which introduces the infection may destroy and devitalize tissue. If, however, the quantity has been small, the individual with a high defense will very clearly stamp out that infection in a very short time. When a few living streptococci are placed in normal blood, the chances for their proliferating are very small, for the factor of safety of a normal individual is relatively very high. If it had not been so, few of us would have survived any of ten thousand battles which have occured within our bodies.

But each individual has a first line defensive mechanism which corresponds with a police duty, ample to take care of individual ruffians or intruders. When, however, a rebellious mob attacks the community, the state militia is called out, which, however, is a reaction of the community that occurs only in the presence of a serious invasion of the community's rights; and if, perchance, the violent invaders of the law cannot be subjected by the state militia, the national army will be called into service. But just as the state militia will not be called upon until the state peace is endangered, just so the national army will not be called upon until the national peace is endangered, or until the defensive process gets beyond the capacity of the smaller unit of defense. The circulating blood and lymph have an adequate defense for taking care of a few invading organisms; and if they should get past a first line defense, every tissue of the body has a defense against them as well as its own reserve. A small infection will not call forth a large defensive reaction any more than a single burglar will call forth the state militia. There must be a riot call for the secondary defense; and when the blood serum and body lymph cannot combat the infection, a system with an adequate defensive organization will so signal through the nerves and chemotactic mechanisms that the reserves will be called out.

Just here we come to one of the most fundamental of the processes. The reserves of the body are carried in circulating glands which are passing to every tissue of the body, carrying what we might think of as fire extinguishers, not used until the occasion demands. These circulating glands are the leucocytes. They are, perhaps, Nature's most wonderful mechanisms, for the list of accessories they furnish is large. Within one minute after living or dead organisms are placed in normal blood, whether circulating in the body or out in the test tube, their presence in the blood will call forth from these leucocytes, chemicals which will destroy those invading organisms in very large numbers. They are the state militia, but unlike the state militia are omnipresent, being ready for a riot call at any place at any time.

But just here comes the great difference between the various individuals that make up society. Whereas some individuals furnish a blood plasma that will kill quite a large number of organisms without calling upon the reserve forces of the leucocytes, other individuals have a very low capacity for killing; in other words, there is a very low bactericidal property to the blood serum and the lymph. This is clearly shown by heating the blood of those individuals, when drawn, to 48°C., which, as Wright has shown, kills the leucocytes and leaves the blood only its police force without the privilege of calling upon its state militia, to use our simile. With some individuals the calling forth of this secondary defensive mechanism will be accomplished with a very slight invasion. These are the people who, when they have a cold or Flu, have it sharply for a day or two and they are over it; or if they have an abscessed tooth, it swells violently and there is a profuse discharge, they have a high temperature, are greatly prostrated for a short period, but are over it quickly. Their prostration is in a sense a measure of the promptness of their reaction and the completeness and speediness with which they have split the foreign protein, which, incidentally, is momentarily poisoning their whole system until it is eliminated.

We have thought of the defensive mechanism of the leucocytes largely in terms of their capacity to phagocyte. I have shown in Chapter 41, Variations in the Defensive Factors of the Blood, as have also others, that the blood of a normal individual will devitalize a vigorous vital culture so that but a small fraction, in many instances, of the total quantity of organisms will grow after being subjected to that blood for the small space of time of one minute; whereas, if this blood were heated to 48°C. for one minute, which would kill the leucocytes, very few of the organisms would be destroyed.

Another and most important phase is the following: We think of defensive reactions as we do chemical reactions, that a small defense will take care of a few organisms; and if more organisms shall invade the blood stream, results will always be a measure of the defensive capacity; in other words, that defense is always quantitative in its relation to invasion. But Wright has shown that this is not the case, which facts we have verified in our work. With small doses of infection applied to blood *in vitro*, a very low percentage of these organisms may be devitalized; whereas, in that same blood, it may be that the addition of a larger dose will increase the reactivity from, let us say, a few per cent less than 10 in the first instance to over 99 per cent with the larger dose. (See the illustration in Figure 248.) In that case it will be seen that after inoculation of the blood with one thousand dead organisms for twenty minutes, it was able to destroy approximately 99 per cent of a thousand live ones which were exposed to it for only ten minutes and then placed in culture media. This is one of the most marvelous illustrations of chemotactic reaction that we know of in all biology; and it is most striking that this very difference is just as clear cut when the test is applied to the blood of our patients with a defective or deficient defense. Such a condition is shown in Figure 248. This, then, becomes not only a means for determining quite rapidly the measure of the patient's capacity for defending himself or herself against dental infections, but also gives a means for determining whether a vaccine made of these dead organisms will be helpful to that patient and in what dosage the vaccine will be most helpful. I have shown in the figures of that chapter the relative efficiency of vaccines made by different methods. If the blood of a given individual reveals, on making these, that the donor does not have within the blood even a capacity for reaction, regardless of the size of the vaccinating dose, the process of vaccination can only be harmful; and this in all probability explains why such variable results have been obtained by the use of vaccines. In my own hands I have had most discouraging results in some cases and most encouraging in others. Many of each of these will be referred to in the succeeding chapters.

For those individuals who do not have a capacity for rallying a depressed defensive reaction, the prognosis is very bad. Whether this condition is the result of a vicious cycle set up by the organisms is not clear. There is a strong suggestion, however, that it relates both to type of organism and to type of defense. These are the individuals who frequently have recurring rheumatic group attacks, very often involving the heart, and from which they never entirely recover though at times seeming relatively free. When in the attacks, the streptococci can nearly always be grown from their blood. The question as to how long this state will exist and whether they will some day regain a defense is problematic. For many of them the prognosis must be guarded and the condition considered serious, if not grave. But just here we see the need for intensive research on an adequately comprehensive scale to develop a chemotactic means for supplying to these patients what they do not already possess or the mechanisms to create. For some, blood transfusions will be helpful, but usually temporarily so, if the state is a chronic one. The data I am developing on this phase of the problem is not ready for presentation but will be presented in a separate communication.

In the succeeding chapters of this book, constituting the second part, I will review case histories and clinical data relating to a large number of groups of affections which more or less frequently disturb humanity. Unfortunately, the prevalence of these disturbances is very much greater and the incidence very much more suttle and of longer standing than has been anticipated. I have spoken of these as the *rheumatic group lesions*. It seems probable that we will come more and more to speak of them as the *degenerative diseases*, since they constitute the slow loss of function, with structural degeneration, of various organs and tissues of the body. The government statistics speak of them frequently as *old age diseases*, and it is pathetic that so many individuals are slowly dying of old age diseases anywhere from thirty years on.

But this raises the question as to the etiology of these old age or degenerative diseases. We have thought of endocarditis, nephritis, cholecystitis, etc., particularly the first, as being the result of an accidental invasion of the body by an organism which has attacked the heart or other involved tissue, or, perchance, that the individual was born with a defective heart. It is most tragic that, whereas the death rate has been reduced in the acute infectious diseases, it not only has not been decreased in the degenerative diseases but in some instances and communities seems definitely to be on the increase. If the placing of an infected tooth beneath the skin of a rabbit can in weeks, months, or a year, (illustrations of which we have produced), develop a typical nephritis in a rabbit where the tooth was taken from a patient suffering from nephritis, (we have evidence indicating that the teeth of individuals without apparent nephritis may also produce nephritis in rabbits, though not in so large per cent,) it then becomes a matter of great concern and responsibility that in those communities and in the groups of individuals with most focal dental infections, the incidence of these degenerative diseases is greatest. Perhaps no lesson of greater import to the health of the nation has come out of these various studies than the fact, that in our hundreds of carefully taken case histories, as shown in Chapter 4, incidence of these degenerative diseases is many fold greater in those individuals with known focal dental infection than those known to be free from dental infection. I am not presuming that these may not be associated factors in part, but I am satisfied that they are, in addition, contributing factors, the latter to the former.

I will, therefore, urge that the members of the dental profession will keep this thought in mind as they review the many cases of degenerative diseases presented in the subsequent chapters and that they shall note the large number of instances in which even so severe conditions as critical heart involvements have quite completely subsided and remained quiescent for years by the removal of dental focal infection, and also the high incidence in which the infection from these dental infections produced comparable lesions in experimental animals; and, as you read, I beg of you to keep in mind and note critically how almost invariably the dental focal infection existed about a tooth which was entirely comfortable and from the old standards of valuation was efficient and safe, notwithstanding its demonstrated potential capacity for harm. I also beg permission to suggest to physicians, who will read this, that they recognize first that teeth may have an almost incalculable value either for mastication or the retention of mechanisms for mastication, and it is a harm that can scarcely be estimated to remove teeth that are not injuring the individual, for in many instances we have seen individuals doomed to two crutches instead of one, by making them dental cripples without doing the slightest benefit to their dental conditions, or for lack of an adequate interpretation and diagnosis.

There is a phase of the process of immunity which we have but little understood, namely the injurious effects resulting from long maintained defensive reaction. We can readily understand, for example, how the persistent use of water to prevent combustion would probably introduce injurious disturbances of an entirely different kind than those we are seeking to combat. We have seen how the very process by which nature tends to neutralize imperfectly reduced acid products, may deplete the body of bases essential for organ tissue functioning, such for example as calcium, thereby depleting the tissues of the ionic calcium required for metabolic processes. The development of these acid products may be produced by many individual or combined forces, a very important one being improper food intake. There is, however, a role in which dental infections enter very directly into this problem, for, as we have demonstrated, the placing of an infected tooth beneath the skin of a rabbit may act very directly upon the acid-base balance of the animal. In the succeeding chapters in Volume Two we will see many cases where the alkalinity index progressed rapidly toward normal with the removal of dental infections. Few, if any, of the forces producing disturbed function and organ and tissue degeneration, are so important as are the forces disturbing the acid-base balance. I have shown that when rabbits are chilled for a few minutes in ice water they will develop suppurative arthritis from an inoculation of dental infection so small as to produce practically no effect on the control animals not chilled. The chilling of these animals disturbs the local circulation, thus preventing a normal drainage from the tissues of the acid products of catabolism, which should normally be transported regularly and rapidly through the blood, carried by the erythrocytes and discharged largely through the lungs as carbon dioxide. One can get a simple demonstration of the small amount of retained acid products that will do harm, the oxidation of which is accomplished by the inhaled oxygen, by ceasing to breathe for a few minutes and noting the distress. This is just as true of any isolated tissue as when it involves the entire organism. The war experience has demonstrated that the compression of blood vessels by the placing of tourniquets, caused the accumulation in that limb, in which the circulation was cut off, of acid products which depleted the alkali reserve of not only those tissues, but also of the entire body, when the circulation was re-established, resulting in profound and often fatal shock from acidosis. Indeed it now seems demonstrated that shock is largely, if not chiefly, the result of such disturbances in the acid-base relationships. When these processes develop slowly, there is a distinctly different type of disturbance. The individual suffers a sense of depression and lassitude characterized by special organ disfunctions, which disfunctions are fundamentally due to organ and tissue change, the extent of which is the measure of organ and tissue degeneration. If, as seems indicated if not demonstrated, infected teeth carry toxic substances capable of directly disturbing the acid-base balance by means of a substance or substances in many respects resembling guanidin, they are potentially of prime importance in the production of organ and tissue disfunctions, degeneration, and chronic shock.

Dental infections are thereby of double importance since they play this dual role, for in addition to this direct effect upon the blood, they produce acute and chronic changes in blood vessel walls often resulting in their spontaneous perforation, and develop bacterial invasions with local necrosis. In short, we find an infected dental tooth to be an enemy fortress within the tissues of the host from which, by these various processes, the invading organisms may break down with progressive degenerative processes various of the organs and the tissues of the body, while the host is virtually helpless to defend itself because of their insidious methods of warfare.

The detailed study of a large number of typical and illustrative cases with special references to their clinical aspects, will constitute the second part of this presentation, which is placed under a separate cover as Volume Two. This division of the work into two units has become necessary owing to the difficulty of handling so large a volume.

I will, accordingly, summarize the phenomena of immunity and susceptibility from streptococcal infections briefly as follows:

1. Dental infections are essentially battle grounds between protected invading streptococcal infections and a more or less efficiently reacting host. The capacity for reaction on the part of the host determines the appearance of the battle ground in the local zone and the depredations of the sneaking invaders in the systemic zones.

2. The capacities of the host for making an adequate warfare are determinable qualities relating to the body fluids, chiefly to the blood.

3. The degenerative diseases have their origin in part, and I fear in quite large part, in dental focal infections.

3. The most important step that can be taken for the still greater improvement of the health of the nation can, in my belief, be had in the systematic prevention of focal infections, of which the dental group constitutes by far the largest proportion.

CHAPTER LVII.

GENERAL SUMMARY AND RESTATEMENT OF FUNDAMENTALS.

INTRODUCTION.

If my interpretations of the preceding researches are correct, there is need for a recasting of the fundamentals for diagnosis, prognosis, and treatment; and I am not unmindful of the tremendous responsibility that I am assuming in suggesting a new alignment of these fundamental principles. It has been because of a recognition of this tremendous responsibility that I have refrained from publishing these data until after I have had a chance to test them out on not a few hundred but on many hundreds of cases, and my presumption and my final willingness to do so are based entirely upon my personal confidence that they are correct. I do not assume that my interpretations are in every detail as later information will indicate, but in the light of present knowledge, they seem to me to be the most logical, and I feel it my duty to give them to humanity and the professions in order that others may assist me in correcting and enlarging them as further facts may indicate. I hope to have an opportunity to strengthen or reinterpret with the addition of new data which I am rapidly accumulating. I have no interest or desire that these suggestions shall prevail, except as they may be found to be based upon truth, and he will be my most kind friend who will furnish data to establish their incorrectness.

I have, accordingly, for simplicity and clearness undertaken to make a brief statement of the old, or generally accepted, interpretations and have placed these in one column, and have placed in a parallel column what I would deem to be a more nearly correct interpretation in the light of the available data. I do not presume that all members of the profession are at present interpreting these fundamentals as I am wording them in the old viewpoint. I believe, however, that the great majority of the members of the healing professions do so interpret; and no one will be more glad than myself if I be in error in this conviction. The following is a statement of the old and the new interpretations as I have suggested them.

The preceding research problems cover the fundamentals that have been in general consideration in problems of dental diagnosis, prognosis, and treatment. My researches upon them have opened up many additional problems, twenty-seven of which I have presented in the latter part of the preceding chapters. There cannot, therefore, be given for these latter problems, an old and a new interpretation. I will, accordingly, present herewith, some general interpretations growing out of the general applications and later researches, and in place of the statement of the problem as an old fundamental in the left hand column as in the first seventeen chapters, will simply state the problem.

NO. 1. ROENTGEN-RAY LIMITATIONS.

OLD INTERPRETATIONS	NEW INTERPRETATIONS
(a) Roentgenograms of teeth will reveal the presence of infection.	**(a) Roentgenograms do not reveal infection, and may or may not reveal its effects.**
(b) The apparent extent of the absorption is the extent of the infection.	**(b) The extent of the absorption does not express the extent of the infection, except in part as that individual's reaction to the infection is understood.**
(c) An area of absorption, if present, can be disclosed by the roentgenogram.	**(c) An area of absorption of the supporting tissue at the apex of a tooth, or laterally, may not be disclosed because of any of the following conditions: (1) Being hidden by a part of that tooth, such as another root; (2) A heavy mass of bone, such as the malar bone; (3) A layer of condensing osteitis obscuring the rarefying osteitis.**

NO. 2. BACTERIAL CAUSE.

If dental infections produce disturbance in other parts of the body, it is because the organism that has chanced to invade that tissue is one having the specific qualities for that invasion and localization regardless of the host, much as the organisms of erysipelas and mumps will respectively select the skin and parotid gland.	**Dental infections involving root canals and their apices and supporting structures practically always contain streptococci, of which, biologically, there are many types or strains, any one of which may be the important causative factor for any of the various types of rheumatic group lesions, regardless of biological classification. The elective localization and attacking qualities are developed by the environment and are, consequently, a factor of the soil or host.**

NO. 3. LOCAL ORAL STRUCTURAL CHANGES.

OLD INTERPRETATIONS	NEW INTERPRETATIONS
(a) Dental infection in bone will express itself as absorption. *(b) A given dental infection will express itself in the local tissues of the mouth approximately the same in all people.*	**(a) Dental infection in bone may express itself as absorption, even extensive absorption, or may be attended by very little or no absorption, or may even produce a marked increase in the density of the bone.** **(b) A given dental infection will not express itself in the local tissues of the mouth approximately the same in all people. People tend to divide into groups with regard to this matter of local reaction, which groups are very dissimilar.**

NO. 4. SYSTEMIC REACTIONS. ARE HUMAN BEINGS COMPARABLE?

Human beings are similar in their susceptibility to reactions to dental infections, or sufficiently so, that they may be considered comparable and be judged by the same standards.	**Human beings do not react with sufficiently uniform similarity to justify the premise that they can all be judged by the same standards and, therefore, may be considered comparable in their susceptibility to systemic involvement from dental infections. They can, however, be divided into groups, the members of which are sufficiently similar to be judged by the same general standards, and they of that group may, therefore, be considered comparable. On the basis of this quality of susceptibility, they readily classify into three groups: namely, those with an inherited susceptibility, those with an acquired susceptibility, and those without a susceptibility to rheumatic group lesions.**

NO. 5. RELATIONSHIPS BETWEEN LOCAL AND SYSTEMIC EXPRESSIONS.

Since, according to the presumption all individuals are similar, and since dental infections are entirely dependent for their characteristics upon the type of organism which has chanced to secure access, therefore there are no characteristics of the local tissue pathology which are related to the degree of susceptibility or nature of systemic involvement.	**Local dental pathology about an infected tooth has variations which make grouping and classification easily possible on this basis, which groups have a direct relationship with similar groupings that can be made on the basis of susceptibility to rheumatic group lesions. The local and systemic expressions are not only related, but are both symptoms of the same controlling forces and conditions.**

NO. 6. VISIBLE ABSORPTION AND TOOTH INFECTION.

OLD INTERPRETATIONS	**NEW INTERPRETATIONS**
(a) A tooth without visible absorption at its apex is not infected.	**(a) Teeth without absorption at their apices can be, and frequently are, infected in the pulp, dentin, and apical tissue.**
(b) A tooth with visible absorption at its apex is infected.	**(b) Teeth with periapical absorption can have the same produced by irritating medication or trauma.**

NO. 7. CARIES AND PULP INFECTION.

Pulps of teeth not exposed by caries are not infected.	**Teeth with moderate caries frequently and with deep caries generally, have their pulps already infected to some extent through this channel.**

NO. 8. PERIODONTOCLASIA AND PULP INFECTION.

Pulps of teeth with pockets from periodontoclasia not involving the apex are not infected.	**Teeth with shallow or moderate pockets from periodontoclasia frequently, and with deep pockets from periodontoclasia usually, have their pulps already infected to some extent from that source.**

NO. 9. CARIES AND SYSTEMIC INVOLVEMENT.

There is no relationship between caries and systemic involvements.	**Susceptibility to dental caries and systemic involvements from dental lesions are proportional, both as cause and effect and as related symptoms.**

NO. 10. PERIODONTOCLASIA AND SYSTEMIC INVOLVEMENT.

With an increase of susceptibility to periodontoclasia, there is a marked increase in susceptibility to rheumatic group lesions.	**Individuals with marked susceptibility to periodontoclasia have, as a group, a decreased susceptibility to the rheumatic group lesions during the period of its active development (in its secondary stages it may contribute to rheumatic group lesions;) or expressed otherwise, individuals with a very marked susceptibility to rheumatic group lesions tend, in general, to be free from extensive periodontoclasia; and when rheumatic susceptibility does develop, it would generally be classed as an acquired factor.**

NO. 11. PERIODONTAL AND APICAL REACTIONS.

OLD INTERPRETATIONS	NEW INTERPRETATIONS
There is no relationship between the extent of apical absorption from a pulp involvement and the presence or absence of a periodontal absorption from a gingival irritation.	**There is a direct relationship between tendency to absorption of alveolar bone in response to irritation, whether at the gingival border or at the root apex; and individuals with extensive periodontoclasia have, for a given dental infection, much more extensive areas of absorption at the apices of infected roots, than do patients without a tendency to periodontoclasia.**

NO. 12. RELATION OF APICAL ABSORPTION TO DANGER.

The quantity or extent of the absorption is a measure of the danger; or otherwise expressed, the size or extent of the disclosed area of absorption at the apex of the root of a tooth is directly an expression of the quantity of infection and, therefore, a measure of the danger from it.	**Since different people react differently, through a wide range, to a given infection, the extent of the area of absorption is not a measure of the danger; but, on the contrary, it may be, and frequently is true that the patient suffering severely from a systemic reaction caused by a dental infection shows very little absorption compared with that which the same dental infection would produce in a patient with ample and high resistance.**

NO. 13. NATURE OF FISTULA DISCHARGE.

Flowing pus from a fistula is, necessarily, very dangerous to the patient since it is an expression of the quantity of local infection and, therefore, a measure of the danger from it.	**Since an adequately active defense against a dental infection, both locally and systemically, produces a vigorous local reaction with attending extensive absorption and the products of inflammatory reaction, namely, exudate and plasma in sufficient quantity to require an overflow, usually spoken of as pus from a fistula, this overflow may be, and usually is, evidence of an active defense and is constituted almost wholly of neutralized products and is often sterile, and such a condition is much more safe than the same infected tooth without such an active local reaction.**

NO. 14. ROOT CANAL MEDICATIONS.

OLD INTERPRETATIONS	NEW INTERPRETATIONS
(*a*) *Infected teeth can be sterilized readily by medication.* (*b*) *Usual medications do not injure the supporting structure.*	(a) **Infected teeth can be completely sterilized in the mouth only with great difficulty, or by the use of medicaments whose irritability readily injures the vitality of the supporting structures of the teeth.** (b) **Many of the usual methods used for the sterilization of infected teeth do serious injury to the supporting structures about the teeth.**

NO. 15. ROOT CANAL FILLINGS.

Root fillings fill pulp canals and continue to do so.	**Root fillings rarely fill pulp canals sufficiently, perfectly to shut out bacteria, completely or permanently. Root fillings usually fill the pulp canal much less perfectly some time after the operation, than at the time of the operation, due to the contraction of the root-filling material. The ultimate volume contraction of the root filling is approximately the amount of solvent used where a solvent is used with gutta-percha as a root-filling material. Infection is a relative matter, and quantity and danger are both related to defense, which defense may vary from high to exceedingly low.**

NO. 16. COMFORT AS A SYMPTOM.

Local comfort and efficiency of treated teeth are an evidence and measure of the success of an operation.	**Local comfort not only is not a certain index of success or safety, but may constitute both what is probably one of the greatest paradoxes and one of the costliest diagnostic mistakes through injury to health, that exists in both dental and medical practice, because it may only mean the absence of local reaction which would, if present, incidentally make the tooth sore and fundamentally destroy the infection at its source whereas, the absence of this local reaction and its consequent destruction of the infection products, permits them to pass throughout the body to irritate and break down that patient's most susceptible tissue, which tissue can be anticipated very frequently, if not generally.**

OLD INTERPRETATIONS

NEW INTERPRETATIONS

NO. 17. CAPACITY FOR INFECTION OF ROOT-FILLED TEETH.

When infected teeth produce disturbance in other parts of the body, it is primarily because the patient is overwhelmed by a large quantity of infection.

When infected teeth produce disturbance in other parts of the body, it is not necessary that the quantity of infection be large, nor is it demonstrated that it is necessary that organisms always pass throughout the body or to the special tissues involved, but the evidence at hand strongly suggests that soluble poisons may pass from the infected teeth to the lymph or blood circulation, or both, and produce systemic disturbances entirely out of proportion to the quantity of poison involved. The evidence indicates that this toxic substance may, under certain conditions, sensitize the body or special tissues, so that very small quantities of the toxin or of the organisms which produce it, may produce very marked reactions and disturbances in that tissue.

NEW PROBLEMS

NO. 18. STUDIES OF PULPLESS TEETH.

Have pulpless teeth injurious contents other than microörganisms?

Infected teeth may contain in addition to microörganisms toxic substances, which produce very profound effects upon experimental animals and which tend to prepare the tissues of the host, at least in some cases, for a more ready invasion by the organisms growing in that tooth.

NO. 19. HEMATOLOGICAL CHANGES IN THE BLOOD.

What changes are produced in the blood and sera of the body by dental infections?

Dental infections may produce very serious changes in the blood and sera of the body, some of the most frequent of which are leucopenia, erythropenia, lymphocytosis, and hemophilia.

NO. 20. CHEMICAL CHANGES OF THE BLOOD.

What are the chemical changes that are produced in the blood by acute and chronic dental focal infections?

Dental focal infections tend to produce, in many instances, one or several chemical changes in the blood, which changes tend also to be produced in animals when an infected tooth is placed beneath its skin, and, similarly, with certain methods of inoculation with the culture grown from these

NEW PROBLEMS	NEW INTERPRETATIONS
	teeth. Some of the changes most frequently found involve: (a) The ionic calcium of the blood. (b) The presence of a pathologically combined quantity of calcium in the blood. (c) A reduction of the alkali reserve of the blood. (d) The development of acidosis. (e) An increase in the blood sugar. (f) An increase in the uric acid. (g) The development of nitrogen retention. (h) The development of products of imperfect oxidation.

NO. 21. CONTRIBUTING OVERLOADS WHICH MODIFY DEFENSIVE FACTORS.

What are the contributing factors causing a break in resistance?	Dental infections, while potentially harmful, may not be causing apparent or serious injury until the individual is subjected to some other overload, at which time a serious break may come. The chief contributing overloads are influenza, pregnancy, lactation, malnutrition, exposure, grief, worry, fear, heredity, and age.

NO. 22. ELECTIVE LOCALIZATION AND TISSUE AND ORGAN SUSCEPTIBILITY PHENOMENA.

Do the organisms of dental infections possess or acquire tissue affinity and elective localization qualities?	Dental infections may or may not contain organisms with a specific elective localization quality for certain tissues of the body. When they do so it is generally because the host is then suffering, or has previously suffered, from an acute process in that tissue, which acute process frequently, entirely and permanently, disappears with the removal of the focus of infection. There is evidence to indicate that the complete removal of an organ so affected does not destroy that elective localization quality in the microörganisms of the focus. Defense and absence of defense to streptococcal infection as an organ and tissue quality, seems definitely to be related to inheritance and, as such, obeys the laws of mendelian characteristics.

NO. 23. ENVIRONMENT PRODUCED BY INFECTED PULPLESS TOOTH.

NEW PROBLEMS	NEW INTERPRETATIONS
What are the characteristics of the habitat and environment furnished for bacteria in an infected pulpless tooth?	**Since an infected tooth is a fortress for bacteria within the tissues of the host, and since, in accordance with the laws governing the behavior of solvents and solutes, the dissolved substances within the tooth can pass to the outside of it, and, similarly, the dissolved substances outside the tooth can pass to the inside of it, together with the fact that the defensive mechanisms of the body are quite unable to enter and reach the bacteria within the tooth except in exceedingly small numbers through the natural openings of the root, which openings will, however, permit the organisms to pass at will from within the tooth to the outside, we must conclude that an infected tooth furnishes a condition and environment that is tremendously in favor of the invading organism inhabiting it, as compared with the host, since the latter may only rid itself of the menace by exfoliating it or absorbing it.**

NO. 24. ELECTIVE LOCALIZATION AND ORGAN DEFENSE.

Do diseased organs and tissues modify bacteria growing in the distant focus, or create in them a capacity for elective localization for those diseased tissues?	**We are led to conclude from the available data, that we do not as yet have sufficient information to draw a close distinction between the influences of the organisms on the affected organ, in contradistinction to the influences of the diseased organ upon the organisms in the focus. The available data suggest strongly, if they do not definitely indicate, that both these conditions exist, in some instances, either one acting entirely alone, and in some others there are indications that both exist at the same time.**

NO. 25. RELATION OF IRRITANT TO TYPE OF REACTION.

Have we different products from dental infection?	**The evidence available indicates that infected teeth elaborate two distinctly different products, one being bacteria, and the other a toxic substance or group of**

NEW PROBLEMS	NEW INTERPRETATIONS
	toxic substances, which, independently of the organisms developing them, may produce various and profound disturbances in tissues in various parts of the body, one of the important group of disturbances being that of the blood stream.

NO. 26. CHEMOTAXIS AS A MEANS FOR INCREASING DEFENSE.

NEW PROBLEMS	NEW INTERPRETATIONS
Can defense for streptococcal infections be increased by introducing enterally or parenterally (by ingesting or injecting) chemicals?	These preliminary experiments would seem to suggest that, means can be developed which will effectually assist, by chemical means in the defense of the body against the invading streptococcal organisms of dental origin or from other sources which produce the rheumatic group lesions.

NO. 27. THE EFFECT OF RADIATION ON DENTAL PATHOLOGICAL LESIONS.

NEW PROBLEMS	NEW INTERPRETATIONS
Can periodontoclasia and apical abscess and inflammation be cured by various types of radiation?	(a) These three forms of radiation—namely, Roentgen-ray, radium radiation, and ultraviolet as generated from mercury vapor and quartz tube—have definite effect on cell resistance and proliferation, and thus directly upon tissue reaction expressions such as pus, bacterial invasion, and granulation. (b) Some of these forces are apparently definitely harmful; others are apparently definitely helpful.

NO. 28. GINGIVAL INFECTIONS, THEIR PATHOLOGY AND SIGNIFICANCE.

NEW PROBLEMS	NEW INTERPRETATIONS
Are the present theories regarding the etiology of periodontoclasia, or so-called pyorrhea alveolaris, correct?	(a) Inflammatory processes of the tissues about the teeth are a direct expression, and therefore a measure of the vital capacity for reaction of that individual to an irritant, during those stages of these lesions, characterized by an abnormally high vital reaction. (b) The individual, who has had this capacity for a very active reaction to the presence of irritants, may pass into a condition or state in which he or she has lost that high defensive factor, at which time sev-

eral changes develop, including a cessation of the absorption of alveolar bone, a lowering of the alkalinity of the periodontoclasia pockets, a change in their bacterial flora, all of which may provide under these later conditions a focus for systemic infection of the most dangerous type, though they may have ceased to have evidence either of local inflammatory disturbance, or exudate as pus.

(c) To the ordinary observer, lay or professional, these two very dissimilar states are considered to be similar or identical though they are potentially very different.

(d) These different peridental expressions or reactions to irritations are accompanied by, and doubtless related to, changes in the ionic calcium and alkali reserve of the blood.

NO. 29. ETIOLOGICAL FACTORS IN DENTAL CARIES.

What are the dominant etiological factors in dental caries?	Dental caries is dependent upon the following factors: (a) A reduction in the hydrogen ion concentration of the normal environment of the tooth. (b) An acid producing bacterium. (c) A change in the chemical constituents of the pabulum bathing the tooth.

NO. 30. THE NATURE OF SENSITIZATION REACTIONS.

Do dental infections produce sensitizations of an anaphylactic character?	(a) Teeth contain substances other than bacteria to which the individual may become sensitized, and which substances may, in addition, have strong toxic properties. (b) The evidence here presented suggests that dental infections are capable of producing in an individual a state of anaphylactic sensitization, which condition may entirely and apparently permanently disappear with the removal of the dental infections. These disturbances may occur in dermal tissues, mucous membranes of the nose and throat, lacrimal tissues, mucous membranes of the bronchioles and air passages, as asthma, and the mucous mem-

NEW PROBLEMS	NEW INTERPRETATIONS
	branes of the digestive tract and a number of other types of tissues.

NO. 31. PRECANCEROUS SKIN IRRITATIONS.

Are there relationships between precancerous skin irritations and dental infections?	**The evidence available suggests:** **(a) That dental infections may produce localized anaphylactic reactions, as irritations of the skin and mucous membranes.** **(b) That these sensitizations may develop into precancerous conditions.**

NO. 32. DENTAL INFECTIONS AND CARBOHYDRATE METABOLISM.

What, if any, is the relationship between dental infections and carbohydrate metabolism?	**Dental infections may produce marked changes in carbohydrate metabolism and probably structural and degenerative changes in the islets of Langerhans of the pancreas, with the production of hyperglycemia and glycosuria.**

NO. 33. MARASMUS.

Why do people with rheumatic group lesions tend to be underweight?	**Dental infections, when they affect the patient systemically, frequently, if not generally, produce a depression of the individual's weight; and marasmus, whether mild or severe, may be considered one of the diagnostic symptoms in studying the relation of dental infections to general health.**

NO. 34. PREGNANCY COMPLICATIONS.

Do dental infections have a bearing on pregnancy complications?	**(a) These researches have shown that in animals, infections from dental origin may have a very far-reaching effect on each the expectant mother and her fetus, which latter may be prematurely expelled or may be rendered lifeless.** **(b) Inasmuch as a large number of our serious cases of rheumatism, heart, and kidney involvements, have their origin at the time of pregnancy in humans, in which cases our clinical histories show that there have been present extensive dental focal infections, it is suggested as important, if not improbable, that expectant mothers shall be free from dental focal infections, both for their own safety and efficiency and for the continued vitality of the fetus.**

NO. 35. SPIROCHETE AND AMEBA INFECTIONS.

NEW PROBLEMS	NEW INTERPRETATIONS
Do organisms other than streptococci enter the human system through dental infections?	**While the streptococcus seems universally to be present in dental infections in practically all cases of systemic involvement, in addition to this variety the evidence seems to establish that both staphylococci and spirochetes may pass from infected teeth to other tissues and proliferate in localized areas; and, similarly, that when certain mixed strains are injected into experimental animals, localized spirochete infections may develop in their tissues. Systemic involvements from spirochete infections and their localization in experimental animals are, however, relatively rare.**

NO. 36. NUTRITION AND RESISTANCE TO INFECTION.

What is the relation of nutrition to resistance to dental infection?	**The data at hand suggest:** **(a) That the effects of variations in the diet do not express themselves quickly in specific defense.** **(b) That variations in diet by the limitation of various vitamines produce effects which, in general, are similar to those of overload.** **(c) Deficiency diets, particularly disturbances resulting in a calcium hunger, tend directly to lower the defense to dental infections.**

NO. 37. THE RELATION OF THE GLANDS OF INTERNAL SECRETION TO DENTAL INFECTIONS AND DEVELOPMENTAL PROCESSES.

What is the relation of the glands of internal secretion to dental infections in developmental processes?	**We would summarize these studies as follows:** **(a) Disfunctions of various of the glands of internal secretion are often very materially corrected, and sometimes completely so, by the removal of dental focal infections.** **(b) Involvements have frequently been produced in similar endocrine tissues of the animals by inoculating them with the cultures from the teeth of the involved patients.**

NEW PROBLEMS	NEW INTERPRETATIONS
	(c) The administration of the extracts of the glands of internal secretion, particularly of the parathyroid, is shown to be of distinct benefit in certain cases of depressed ionic calcium of the blood, due in part to dental focal infections, where this improvement has been absent or slow following the removal of the dental infections. (d) An improvement has been produced in individuals, which we interpret to be due to a stimulation of the pituitary body, which in turn doubtless stimulates other ductless glands and together with them produces a marked change in both physical and mental states.

NO. 38. THE NATURE AND FUNCTION OF THE DENTAL GRANULOMA.

Is the dental granuloma a pus sac and its size a measure of the danger?	(a) The so-called granuloma is a misnomer, for it is a defensive membrane and not a neoplasm. (b) A normally functioning periapical quarantine tissue is Nature's effective mechanism for protecting that individual by destroying the organisms and toxins immediately at their source, thereby completely preventing the tissues of that individual's body from exposure to either of these agencies.

NO. 39. CHANGES IN THE SUPPORTING STRUCTURES OF THE TEETH, DUE TO INFECTION AND IRRITATION PROCESSES.

What are the changes produced in the supporting structures of the teeth, which are due to infection and irritation processes?	Characteristic localized structural changes develop in the supporting structures of teeth when the latter carry infection within their structures. These changes are, however, determined chiefly by the host and are an expression of the reacting characteristics of the host rather than an expression of the invading bacterium.

NO. 40. DENTAL INVOLVEMENTS CAUSED BY ARTHRITIS.

Can arthritic infections of the body attack and devitalize the teeth?	(a) It will be seen from these data that a systemic involvement of multiple arthritis may, while attacking various joints of the

body, also attack those of the joints of the teeth; and, further, that this process of inflammation with degenerative and proliferative processes may cause the involvement and ultimate death of the pulp.

(b) The involvement of these teeth as a result of the progressive systemic arthritis may in turn, and doubtless frequently, if not generally, does aggravate the general condition, for the tooth structure when it becomes infected is even less capable of vascularization and therefore less amenable to the processes of defense than is bone. This stresses the very great importance that individuals having deforming arthritis shall have most careful dental inspection and care, and also, since it is one of the most horrible of living deaths, every effort should be made to prevent the beginning of that process; and since the evidence is so overwhelming that the initial infection frequently, if not generally, comes from the teeth, helpless humanity deserves pity until the powers that be shall make a worthy effort to find the means that will prevent this needless catastrophe in so many lives.

NO. 41. VARIATIONS IN THE DEFENSIVE FACTORS OF THE BLOOD.

Is there a difference in the defensive factors of the blood of susceptible and non-susceptible individuals to systemic involvements from dental infections?	There is a marked difference, which is very readily measurable in the bactericidal properties of the bloods of individuals of high defense, as compared with those of low defense to systemic involvements from dental infections.

NO. 42. METHODS FOR REINFORCING A DEFICIENT DEFENSE.

Can a temporarily or permanently low defense against the streptococci of dental infections be increased or enhanced either temporarily or permanently?	In some individuals a low defense may be materially strengthened by the use of vaccines and also by the use of all available means for stimulating metabolism and increasing a supply of essential nutritional factors.

NO. 43. SEROPHYTIC MICROÖRGANISMS.

NEW PROBLEMS	NEW INTERPRETATIONS
What are the growth factors of microörganisms of the mouth in juices of living tissues?	When the mixed flora of the oral cavity are planted in the normal blood serum or lymph, the varieties that grow are almost entirely limited to the strains of diplo- and strepto-cocci, with occasional staphylococci, with the diplo- and strepto-cocci largely predominating.

NO. 44. CALCIUM AND ACID-ALKALI BALANCE.

What is the role of calcium in the maintenance of the acid-alkali balance of the blood, other body fluids, and tissues?	In the proper functioning of the body, the end products of metabolism are carbon dioxide, urea, and water. When metabolic functions are abnormal, resulting in the imperfect oxidation with the development of less simple acids than carbon dioxide, these must be neutralized with bases taken from the body and its fluids. In the absence of an adequate supply of these from other sources, the demand must be met by the calcium of the body, first from the circulating ionic calcium, then from the calcified tissues. This latter is the characteristic end reaction involved in periodontoclasia, or pyorrhea alveolaris. This enters into and complicates the etiology of many, if not most, of the rheumatic group disturbances studied in detail in subsequent chapters.

NO. 45. SYMPTOMS AND DANGER.

OLD INTERPRETATION	
Since individuals are similar in their reactions to dental infections, both locally and systemically, and since freedom from involvements is dependable, the danger is proportional to the quantity and to the type or virulence of the dental infection involved and the patient's symptoms.	Since patients largely determine the biological qualities of the organisms involved in dental infections by the culture medium they furnish the bacteria, and since the sufficiently high defense of certain individuals will, under ordinary conditions, protect them from systemic injury resulting from their dental infections, and since the local oral expressions of the dental infection are an indication and a measure of that individual's reaction to the dental infection rather than a measure of that

infection, therefore, it becomes apparent that the operation that is indicated is an individual factor and concerns the relation of the efficiency of the patient's defense to the attacking power of the dental infections and, accordingly, operations which are strongly indicated for some individuals are as strongly contraindicated for others.

NO. 46. DIAGNOSIS.

An adequate procedure for making dental diagnosis is a orentgenographic study of the patient, for which the only requisite training is a working knowledge of the apparatus and a familiarity with dental anatomy sufficient properly to call the teeth by their names.

An adequate procedure for making a dental diagnosis will involve, as a minimum, the following:

A knowledge of the patient's systemic defense and systemic involvements, both present and past. The securing of this will involve:

(a) A knowledge of the various systemic disturbances that may be produced or aggravated by the dental infection, with or without the patient's recognition of their existence. A knowledge of the systemic disturbances includes, for differentiating purposes, a knowledge of the etiological pathology of the involved tissues of most of the morbid conditions of the human body, regardless of the type of tissue or the involved nature of the functions. These are based upon a thorough knowledge of the gross and minute anatomy of the various organs and tissues of the body, and the normal functions of those tissues, with special reference to the nervous system.

(b) A roentgenographic study, with a knowledge that it is physically impossible for the Roentgen-rays to disclose much of the essential information, the roentgenogram being simply a record of relative total densities of the planes involved.

(c) A familiarity with the use of the microscope and such laboratory technique as serological study of the fluids of the body, since many of the lesions, being produced or aggravated by dental infections, are in evidence by microscopic and chemical methods long before they appear clinically as symptoms.

NO. 47. DIAGNOSTICIANS.

Dental diagnosis is so simple that any dentist or physician, osteopath, chiropractor, electrical engineer, or laboratory assistant, is competent to perform this simple service.

Dental diagnosis is so intricate and involved that it requires a greater knowledge of the human body, its structure and diseases, and of the various means for understanding the normality and abnormality of the same, than any specialty of the healing arts; and probably no specialty finds such great opportunity for doing injury to humanity, or for extending human life, as does the highest application of intelligence in this field. A competent diagnostician of the local and systemic expressions of dental infections must be familiar with the clinical and structural pathology required for a general medical diagnosis, and, in addition, be completely familiar with dental anatomy, dental pathology, and dental operative procedure.

This paragraph completes this presentation of researches on the fundamentals of oral and systemic expressions of dental infections. The practical application of these new interpretations is a continuation of the report of these researches and for convenience has been placed in a separate book as Volume Two, as Chapters 58 to 73. These will consider the role of dental infections in the development and progress of the degenerative diseases.

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